We dedicate this textbook to those who have supported us and shown us the way:

- My grandmother, who lived independently until her mid-90s; my parents, who made my dream of becoming a pharmacist possible; my husband, whose love continues to support me; and my mentors, who encouraged me to be a pioneer in the practice of clinical pharmacy. — LCH

- My father Kenneth, through whose career as a nursing facility administrator I was first exposed to long-term care; my husband Brian, who is my greatest source of love and support and also a fellow pharmacist who well understands my passion for this subject; and to my students, who inspire me daily and who will one day care for us all. — RBS

- The senior patients who have taught us the most about the use of medications. They continue to inspire us through their lives and words.
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In January 2010, a social demographic change began in the United States as the Baby Boomer generation began to turn 65 years of age. Persons near or across this threshold are likely to claim that chronological age is not reflective of their true age and vitality. If being 50 is the new 35, what does that make 75? Aging or being “old” is not a well accepted or welcomed stage of life in our culture. Anti-aging therapies, ranging from skin creams that affect cosmetic appearance to individualized hormone regimens that increase or maintain muscle mass and vitality and diminish the appearance of age, dominate the market and media spotlight while shaping the national conscience of how we think about aging. It is unfortunate and damaging that such an industry can delude the public and tarnish the real champions—older adults. Pharmacists have a role in setting this record straight.

The golden age of geriatric clinical pharmacology was the 1970s and 1980s, when basic age-associated pharmacokinetic and pharmacodynamics changes were identified. Since then, information on the efficacy and safety of new drugs, and how to dose and monitor them, has been generated by pharmacoepidemiologic studies, pooled, and secondary analyses of trials of persons above a certain age included in the trials. The pearls of geriatric pharmacotherapy are not generated from such trials and findings, but by experienced and intellectually curious clinicians and scientists such as those chosen to contribute to this text.

To my knowledge, the first recognized pharmacist-leaders in geriatrics were Ron Stewart and the late Peter Lamy. Their contributed works and mentorship directly affected many of the authors of this textbook. That the field of geriatrics has been atrophying is well documented: training programs continue to decline in number, geriatrics continues to be underemphasized in curriculums, and practices cannot survive on Medicare alone. All workforce predictions conclude that the U.S. healthcare education system cannot train enough pharmacists, physicians’ nurses, and other professionals to meet the demand. Thus, all healthcare providers, including pharmacists, must have working competencies in geriatrics to care for the nation’s aging population. That is where this text can be of great value and contribution.

Once again divided into two sections, General Social, Ethical, Economic, and Biomedical Issues of Aging, and Pharmacotherapy Issues of Aging, the second edition of Fundamentals of Geriatric Pharmacotherapy provides a comprehensive knowledge and reference for both novices and experienced clinicians. For the second edition, each chapter has been updated and several expanded, notably Palliative and Hospice Care. Each chapter includes learning objectives that will be useful for educators and self-learners. Geriatrics, like all specialties, has its own language, and the key terms defined in each chapter compose a helpful glossary for understanding this language. Rather than a stand-alone chapter on demographics, the chapter Challenges in Geriatric Care nicely integrates terminology with demographic changes and puts chronological age into context with other variables that must be considered when providing care for the older patient. The clinical pearls, key points, cases, and questions in each chapter provide the reader with clinical insight not found in clinical trials, meta-analyses, or systematic reviews. The case histories accurately represent the complexity and decision-making encountered when caring for geriatric patients in a variety of clinical settings, providing especially good exposure for the student reader. How to interpret and critique clinical trials for their geriatric content and implications for care are discussed in detail, with examples in several chapters.

As the risk-benefit ratio for patients shifts and goals of care change, knowing when to stop a medication can be just as critical as knowing when to start it. As we age, our heterogeneity increases, i.e., we become less like one another, and our differences are magnified. These points are not lost in the text.

Medication management can be a complex and comprehensive task for patients, caregivers, and families. The challenges for pharmacists, physicians, nurses, and others are similarly complex and time-consuming and often require in-depth reviews of a patient’s history; home visits; an understanding of the patient’s and
family’s knowledge and belief about medications; and assessments of function, cognition, and social support as well as contacting multiple prescribers. The time and energy required to accomplish these tasks are enormous and exhausting. These challenges and the tools to address them are presented throughout the text, along with the pharmacotherapy for treating the diseases, conditions, and syndromes encountered when caring for geriatric patients.

The American Society of Health-System Pharmacists, editors Drs. Lisa Hutchison and Rebecca Sleeper, and all the contributing authors are to be congratulated for their commitment to updating *Fundamentals of Geriatric Pharmacotherapy*. Readers and users should not be exclusively pharmacists but all healthcare professionals who prescribe or have a desire to know more about this important component of geriatric caregiving. Pharmacists, pharmacy educators, and students will find the text a beneficial tool in attaining or teaching geriatric competencies.

Where will future leaders in geriatric pharmacy come from? Hopefully, the continued availability of this text will inspire, stimulate, and nurture them.

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The older population is growing. The U.S. Census Bureau projects the world’s 65-and-older population will double by the year 2050, and the 85-and-older population will increase fivefold in the same time period. With elderly patients come special healthcare needs, and the professional healthcare workforce must be prepared. More and better focused information on geriatrics must be disseminated to healthcare providers.

For most patient populations, providers refer to evidence-based guidelines and the studies on which they are based to provide the best pharmacotherapy for patients. This practice assumes that elderly subjects are well represented in the study populations; however, most trials exclude elderly participants, especially participants who have multiple disease states, are frail, or are more susceptible to rare adverse effects. The risk-benefit ratio may be skewed in these patients, particularly those who are nearing the century mark. This text is designed to build on content that would be delivered in a general pharmacotherapy text. The learner’s foundational knowledge of disease-specific pathophysiology and pharmacology is assumed, allowing this book to focus on evidence published in the elderly population, stressing the differences that are seen across the continuum of young-old, middle-old, and the oldest old.

This textbook is divided into two sections. Section I provides general concepts: biomedical principles of aging, social/behavioral issues, ethical considerations, approaches to geriatric assessment, adverse drug events, and suboptimal prescribing are addressed. There is also a new chapter on palliative and hospice care. Along with updating information in these chapters, we felt that combining the information on adverse drug events and suboptimal prescribing, while incorporating new information on medication therapy management, would strengthen the reader’s understanding of medication review specific to geriatric patients. This foundational material ensures the knowledge base required for a general approach. Section II, which is the bulk of the book, covers disease states commonly encountered in the aging adult and reviews age-specific epidemiology and evidence for treatment in the different senior populations. Common problems and clinical controversies encountered when treating elderly patients are described, with suggested methods to minimize their occurrence. Another new chapter focuses on major infections, with detailed descriptions of the changes in the immune system and ways to ensure proper antimicrobial stewardship for older adults, especially those in long-term care settings.

Every chapter includes key terms, learning objectives, key points, patient cases, clinical pearls, and self-assessment questions that help guide the student through the maze of information required in caring for an older patient. In addition, web-based materials such as course outlines and lesson plans are available to facilitate incorporation of the textbook into course delivery. As a contributed work, we have solicited the expertise of authors and reviewers who practice in the care of elderly patients or who mentor learners in pharmacy or other health professions in the mastery of geriatric pharmacotherapy content.

Although designed primarily as a textbook for pharmacy students to use in an elective or required course focused on geriatric pharmacotherapy, this book is also useful for practicing pharmacists and other healthcare providers who wish to learn more about pharmacotherapy for the elderly patient. The use of medications continues to be one of the most difficult aspects of geriatric practice, regardless of the professional discipline.

It is our fondest hope that this book will serve as a mechanism for pharmacists and other clinicians to improve the use of medications in their older adult patients so they may experience the longest life possible coupled with fullest quality of life.

Lisa C. Hutchison
Rebecca B. Sleeper
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We wish to acknowledge three individuals who reviewed new chapters that were added to this edition. Their wise and thoughtful comments were essential to the quality and clarity of these new chapters:

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PART I

General Social, Ethical, Economic, and Biomedical Issues of Aging

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Learning Objectives

1. Evaluate the applicability of clinical literature to the elderly patient using an approach that is tailored to specific subgroups of the geriatric population.
2. Differentiate the roles of healthcare professionals and the various services and venues available in the care of geriatric patients.
3. Infer scenarios in which geriatric patients are at risk for suboptimal care and intervene when breakdowns in the continuum of care are identified.
4. Recognize the impact of caregiver burden on patient outcomes.

Key Terms and Definitions

ASSISTED LIVING FACILITY: Living environment that provides added services to the individual who is safe to live in the community environment but requires some assistance with various daily activities.

CAREGIVER BURDEN: Psychosocial and physical stress experienced by an individual who provides care to another person.

CERTIFIED GERIATRIC PHARMACIST: Pharmacist who has achieved certification from the Commission for Certification in Geriatric Pharmacy.

CERTIFIED NURSE’S ASSISTANT: Individual who has earned a certificate to practice as a nurse’s assistant and who may work in a wide variety of healthcare settings ranging from long-term care facilities to private homes.

GERIATRIC: Adjective generally used to refer to an older individual.

GERIATRICIAN: Physician with expertise, as demonstrated by fellowship or other added qualifications, in the care of older persons.

GERONTOLOGICAL NURSE: Nurse with expertise, as demonstrated by exam or other added qualifications, in the care of older persons.
**Introduction**

The first challenge in addressing the healthcare needs of a geriatric population is in determining what geriatric actually means. There is not a universally accepted definition. In general, geriatric refers to an older person; however, age is a relative descriptor and may not always apply to various healthcare interventions.

Social or legal definitions of older people are often based on age. For instance, age 65 is commonly considered the threshold age for the geriatric population, and most healthcare literature criteria will use this definition. Government statistics, such as census data, also define older people based on this age, and 65 is the age for eligibility for federal programs such as Medicare. The Food and Drug Administration (FDA) also requires available clinical trial data for individuals over the age of 65 to be included as part of the required labeling for medications. Manufacturers are required to report special considerations for dosage adjustment or avoidance in older patients based on age-related changes in drug metabolism or sensitivity. However, age-based definitions of “older” populations vary. One of the nation’s largest public action groups, the American Association of Retired Persons (AARP), uses a threshold age of 50 years; in contrast, full retirement age for the purposes of Social Security benefits has increased to greater than age 65 and up to age 67 for individuals born after 1960.

Despite a lack of agreement regarding a specific age threshold, there are drawbacks to assuming that all individuals over a given age are the same or have the same healthcare needs. Clinicians would not consider it appropriate to treat a 5-year-old child the same as a 40-year-old adult, as the 35-year span between the two ages is associated with significant developmental changes. Likewise, it would be inappropriate to treat a 65-year-old adult the same as a 100-year-old adult, because they are also at the extremes of a 35-year span. The specific physiologic changes between the two adult patients are distinct from those that separate a child from an adult, but the principle is the same. Failing to recognize the potential for altered response to medication therapy across the age span can result in adverse outcomes.

Therefore, age is only one factor that must be considered within the context of overall health status and functional ability. In addition, despite age or health status, healthcare needs are often addressed very differently depending on the patient’s environment. There are many ways to arrive at a description of the geriatric patient. This presents an inherent problem when it comes to medical decision making for the geriatric patient because it can be difficult to know whether (or how) to apply evidence-based strategies to those individuals who may not actually be represented in the population from which the evidence was derived. Although general treatment principles are important to understand, clinicians must also recognize the heterogeneity of the geriatric population. This presents a tricky balance for our society and healthcare system: providing optimal healthcare to a huge and growing population while recognizing the differing needs of subgroups.
This chapter outlines the distinctions within the geriatric population and presents the many challenges faced by healthcare providers and caregivers in working with this diverse group. It discusses the various roles of the healthcare team and the different care venues. Most importantly, it addresses problems in the healthcare system that allow for suboptimal geriatric care.

**Subpopulations of Elderly Patients**

For practical purposes, there is a need to classify subgroups so that the approach to the elderly patient can be structured and evidence-based yet as specific as possible to individual needs. Interpretation of clinical literature should be performed with these considerations in mind.

There are three primary angles from which to evaluate the applicability of the evidence base to an older patient: age strata, health or functional status, and living/care environment. Each of these can impact the way a health intervention is delivered, how safe or effective it is, or how it can be monitored or evaluated.

**Age Strata**

Sometimes cohorts of subjects in large studies or clinical trials are divided into age strata, and this can be one way of comparing and contrasting health outcomes or treatment effects in subgroups of geriatric patients. For instance, a subject population might be divided into groups by decades, such as 60–70, 71–80, 81–90, or >90. Depending on the body of literature being evaluated, there is also terminology such as *young old* versus *old old* that suggests a similar, albeit more general, stratification of age. The cut-off point between young-old and old-old, though still somewhat arbitrary, is usually age 80–85 years. A focus on the old-old population is becoming increasingly important, given the rapid growth of this segment of the U.S. population.

The biggest challenge in evaluating differences in outcomes between groups is the limitation in statistical power as a result of relatively low enrollment of subjects, particularly in the upper age strata. This can hamper the ability to detect a difference in outcomes for these patients. For this reason, sometimes the most useful information that comes from evaluating the age range of subjects in a study or clinical trial is the recognition of the upper age limit for which there are meaningful data. This can be determined by examining not just the average age of study subjects, but the upper end of the age range reported in a clinical study's subject characteristics. Based on this data ceiling, a clinician must determine whether it is appropriate to assume that an outcome can be extrapolated to the oldest patients.

In addition, age is one of several considerations that are included in estimates of prognosis. The risk-benefit assessment that must occur when deciding whether to implement a medication intervention includes an assessment of how long it is expected for the treatment effect to be realized and whether the individual is likely to live long enough to achieve that benefit, especially if there are risks associated with exposure to the medication.

**Health or Functional Status**

Sometimes, patients with certain comorbidities or disabilities are excluded from research protocols; therefore, clinicians must make judgment calls about the risks and benefits of employing usual treatment in patients with multiple comorbidities or functional deficits. In addition to concerns about how medication therapy outcomes may be altered by drug–disease interactions in an individual with complex comorbidities, there are multiple ways in which functional status can affect the likelihood of achieving the expected therapeutic outcome. Cognitive function and physical function are two domains where deficits can significantly affect medication outcomes. In these cases, the contributions of cognitive status to drug outcomes may be many: individuals with these deficits may be disproportionately vulnerable to drug side effects that exacerbate their
underlying condition, or the deficits may impede the ability to appropriately administer the drug therapy regimen.

An individual with mild cognitive impairment who manages his or her own medication regimen may be vulnerable to poor adherence or medication self-administration errors. Such an individual may also be less able to self-monitor for efficacy and may not appropriately interpret or report potential side effects. Problematic medications may include those with narrow therapeutic windows, such as warfarin, or medications which require a specific technique to administer, such as bisphosphonates. These may be the interventions of choice from a drug–disease standpoint, but their safe use requires consideration of logistical hurdles, which, if not overcome, can tip the balance of benefit to risk.

Similar concerns apply for individuals with deficits in physical function because medication self-administration can be affected by altered vision, coordination, motor function, or swallowing function. Functional deficits may also affect decisions about the appropriateness of medication therapy as it relates to prognosis. For instance, bladder antispasmodics can provide a significant benefit for an individual with urge incontinence, but consider how the ratio of benefit to risk is altered in an individual who is functionally dependent for all his or her personal care and who is dependent on incontinence undergarments despite the use of the medication.

Likewise, a clinical trial that demonstrated a treatment benefit of a medication in an independent-living community population may not achieve the same outcomes in a population of hospitalized patients. Finally, the ability to ensure that a clinical intervention can be implemented and monitored in the same manner as a clinical trial depends on the resources available to the individual in the environment where he or she lives. Does the patient have to drive to an office or clinic to receive care by a health professional? Does he or she qualify for reimbursement to receive services in the home? Does the environment provide medication administration assistance? If so, to what degree? Is there 24-hour supervision for assistance with daily activities and monitoring of health status?

KEY POINT: Subgroups can be defined in numerous ways. Three of the most common are age strata, health or functional status, and living environment.

Applicability of Clinical Literature

When evaluating the applicability of the clinical literature to a geriatric subgroup, several questions should be considered:

1. Are there any studies or clinical trials designed for, or conducted in, populations that mirror the characteristics of the subgroup in question?

2. If not, are there other types of publications involving geriatric patients that might shed light on the nature of medication response? For example, there may be no clinical trials of a medication in elderly populations, but there may be case reports that describe either treatment response or adverse events in older patients.

3. Failing this, broaden the search to literature in the general adult population. Evaluate the inclusion/exclusion criteria or baseline characteristics of the study population. Are there
any subjects included that are representative of the subgroup in question? If so, how many?

It is also important to be careful about interpreting the applicability of consensus guidelines in the adult population for geriatric patients. Consider whether the guideline is specific to older populations or, if not, if there is any elderly-specific language included. If recommendations are made for the older patient, determine whether the guideline identifies specific subgroups of the elderly population or if it suggests that the recommendation is universal to all older patients. Regardless, a good strategy is to evaluate the individual studies cited by the guideline as support for the recommendation. After evaluating the inclusion/exclusion criteria and baseline characteristics of the populations in those studies, determine whether application or extrapolation is appropriate to all older patients.

**KEY POINT:** Scrutinize clinical literature to determine how elderly patients are represented.

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**Venues of Care**

**Who Provides Care?**

Many individuals provide care to older patients. Formal healthcare services are provided by physicians, nurses, pharmacists, and allied health professionals. Specific credentials are not required to care for older patients. In fact, with the exception of those who specialize in pediatrics, almost all health professionals will provide care to older patients regardless of their discipline or practice setting. Based on the growth of the oldest strata of the population, competence in geriatric care will be imperative. However, there is a growing need for a focus or expertise in this area, and various training is available for health professionals wishing to specialize in geriatric care.

**Physicians**

Physicians in almost all areas of specialty will have significant interactions with older patients. Many physicians who have practices largely comprised of older patients may have earned, through experience, significant practical knowledge about meeting the special needs of this population; however, official recognition as a geriatrician implies additional training and certification. There are two primary routes for this. One is through examination, where a certificate in added qualifications in geriatric medicine is available to physicians in the areas of internal medicine or family medicine. Other added qualifications offered by examination include certification in osteopathic geriatrics or geriatric psychiatry. The other route is through fellowship training in geriatrics. A fellowship of 1–3 years in the specialty area of geriatrics is usually completed after residency training in either internal medicine or family medicine.

**Nurses**

Nurses of all levels of training provide care to older patients across a broad spectrum of care venues. There are four certification examinations available for nurses in gerontology, at the associate degree/diploma level or baccalaureate level for registered nurses (RNs), and at the advanced practice level for clinical nurse specialists in gerontological nursing or gerontological nurse practitioners.

Although elderly patients make up 90% of long-term care populations and 80% of home care visits, most of these individuals are not cared for by nurses with these specialty credentials. In many environments, the majority of care is provided or supervised by licensed vocational nurses (LVNs) or certified nurse’s assistants, also called nurse’s aides. In long-term care environments, the majority of staff is made up of nurse’s aides, who provide the day-to-day, hands-on care required by facility residents. Supervision of this care is usually provided by LVNs in the role of charge nurse. RNs usually serve in administrator roles, such as director of nursing, in these environments. Long-term care
regulations require facilities to have at least one full-time RN, but this requirement must often be waived, particularly in rural areas, due to lack of available workforce. Home health agencies or health clinics associated with assisted living facilities (ALFs) or senior housing centers are staffed in a similar way.

**Pharmacists**

Pharmacists provide care to older patients in a variety of settings, and pharmacists in the community setting have perhaps the most frequent opportunities for interactions with older patients. However, one of the most prevalent areas of practice where the focus is geriatric pharmacotherapy is in long-term care facilities (LTCFs). Every licensed LTCF must retain the services of a pharmacist to provide drug regimen review and consultation on other services related to drug acquisition, labeling, storage, security, administration, documentation, and destruction. The primary responsibility of the pharmacist is to identify medication-related problems and to formulate interventions to prevent or resolve them. Pharmacists often provide similar services in ALFs, home-based programs, hospices, and other specialized care settings that focus on the older individual. In the outpatient setting, such as a clinic, pharmacists may see patients in conjunction with a patient's primary care physician. Specific credentials in geriatrics are not required to practice in long-term care or other areas of geriatric practice; however, there are options for obtaining additional training or credentials in this area. Geriatric specialty residencies are available at many institutions, and the Commission for Certification in Geriatric Pharmacy has been offering credentials as a certified geriatric pharmacist since 1997. This certification is voluntary but has become increasingly popular among individuals with a focus on geriatric practice. The process involves an evaluation of education and experience in the principles of geriatric pharmacotherapy and in the provision of pharmaceutical care to the elderly as well as an examination, and periodic recertification is required. The American Society of Consultant Pharmacists provides an educational program that can prepare pharmacists for this exam.

**Other Health Professionals**

Specialized care to address functional deficits associated with morbidity and functional decline is often provided by physical therapists, occupational therapists, and speech therapists. Their services are part of the skilled care that is provided to individuals during or after hospitalization, but it can also be provided as outpatient or home-based care. Physical therapists focus on motor function, range of motion, balance, strength, and endurance. Occupational therapists differ from physical therapists, focusing on the performance of activities of daily living (ADLs). Speech therapists not only address language/communication difficulties but also swallowing function and cognitive skills. Other professionals who provide care to older adults include dietitians, social workers, recreational therapists, and psychologists.

**Interprofessional Teams**

One of the most comprehensive forms of care for an older patient is by an interprofessional team of health professionals. Skilled nursing facilities (SNFs), specialized clinics, hospital systems, or academic health sciences centers may offer the services of a geriatric assessment team. Due to the interprofessional nature of such a team, patients can undergo comprehensive examination, screening, medication review, and other evaluations. Such teams may either serve as the patient's primary source of healthcare follow-up or as consultants providing recommendations from an expert group to the patient's primary physician. The core disciplines in such a team usually include representatives from medicine, nursing, pharmacy, physical therapy, occupational therapy, speech therapy, and social services. Many teams also include dietitians, psychologists, recreational therapists, clergy, or others, based on the patient's needs. Depending on the institution's resources, these teams may also have access to consultation or participation by specialists such as neurologists, cardiologists, psychiatrists, ophthalmologists, podiatrists, or dentists.
Demographics of the Healthcare Workforce

The rapid growth in the geriatric population has been well described. In 2002, one in eight individuals were older than age 65, and this ratio is expected to increase to one in five by the year 2030.11 Unfortunately, the growth of the workforce that is trained to care for these individuals has not been commensurate with this population’s needs.

As of 2011, the number of American Geriatrics Society Board-certified geriatricians was reported as 7,162, a reduction from previous years.12 This is less than 25% of the number estimated to be needed to meet the healthcare needs of today’s population of elderly patients. Although it is understood that a significant amount of care for older patients is provided by physicians who do not seek formal Board certification in this area, since that time there has not been workforce growth commensurate with population growth. Less than 3% of medical students choose to enroll in elective geriatrics coursework.13 Of the 468 first-year fellowship training slots open in 2006–2007, only 54% were filled. There has also been a decline in the number of U.S. medical school graduates entering geriatric fellowships; only about 0.5%. Most physicians entering geriatric fellowships are from medical schools outside the United States; 184 of the 287 physicians entering fellowships in 2007 were international graduates.13 Therefore, most elderly patients do not receive their primary physician care from an individual with these credentials.

In 2003, newly licensed nurses reported that older patients made up 62.5% of their patients.14 However, <1% of RNs and <3% of advance practice nurses are certified in geriatric nursing.15 There is also a shortage of nursing faculty, particularly in geriatric nursing, with 25% of nursing programs lacking a gerontological faculty member.16 In addition to the low numbers of nurses credentialed in geriatrics, there is a shortage of nurses in the healthcare workforce in general. Nurses and nurses’ aides make up the front line of care for the huge population of older patients in almost every healthcare venue described in this chapter, and they are in a position to either provide or oversee a significant proportion of the day-to-day, hands-on care that is delivered. Shortages in the workforce and in the training capacity, particularly in geriatrics, represent one of the most critical areas of weakness in the current health system.17 By 2020, the RN workforce will probably be 20% below that required to meet population needs.

It has been estimated that between 70% and 80% of direct hands-on care of older adults is provided by nurse’s aides, home health aides, and personal care assistants. Training requirements for these direct-care workers differ from state to state. Although there is a federal minimum of 75 hours, this has not been adjusted in over 20 years, and 20 states stipulate only the minimum requirement. The Institute of Medicine (IOM) suggests the minimum requirement be increased to at least 120 hours.17

Pharmacists’ participation in senior care is a growing area of specialty focus. As with other health disciplines, most pharmacists will encounter older patients in their practice regardless of their practice setting, and there are no specialty credentials that are required. Less than half of pharmacy schools have a distinct course in geriatrics.13,17 Accreditation requirements mandate instruction in special populations, but specific criteria for geriatrics curricula are not delineated.18 However, given the significant utilization of drug therapy by the older population and the rising concern with adverse drug outcomes, there is a growing need for pharmacists to serve as patient advocates in this area. Currently, pharmacists who have completed specialty residency training in geriatrics are in short supply, but those who have obtained certification via the Commission for Certification in Geriatric Pharmacy examination are increasing in number.9
KEY POINT: One of the greatest challenges in providing tailored care to elderly patients is the lack of healthcare professionals who are specially trained in geriatrics.

Where Is Care Provided?
The continuum of care for elderly populations includes both chronic and acute care. Chronic care not only includes the day-to-day management of chronic disease states but also may involve the maintenance of ADLs or provision of cognitive supervision. These services can be provided in the home, in ALFs or other specialized senior housing, or in LTCFs.

With respect to acute care, elderly patients make up over 50% of hospitalized populations. Compared to populations under age 65, older patients have longer average lengths of stay, and have special needs in the emergency room or in the hospital. They are particularly vulnerable to adverse outcomes such as delirium or residual disability after acute illness. Rehabilitation services, such as in an SNF, are often required to assist patients in regaining strength and function before being discharged back to the living environment where they receive chronic care. As such, elderly patients are consumers of multiple venues of care.

Home-Based Care
Most individuals prefer to live in their own home for as long as possible; however, declining health can result in disability that makes this difficult or unsafe. It may be possible to continue living in a private home in the community setting provided the proper support is available from either formal or informal caregivers or services.

Informal support is most often provided by a family member, usually a spouse or adult child, but a variety of services for hire can assist an individual with day-to-day needs. This might include assistance with housekeeping, errands, transportation, meal preparation, personal companionship, or other services for which no healthcare professional credentials are required. Individuals with more significant health needs may require assistance with personal care such as bathing, dressing, grooming, toileting, or ambulating. Assistance with medication management is also common. Although individuals often arrange services of this nature with people who are not health professionals, the front line of home-based care is made up of home health agencies. Nurse’s aides may provide day-to-day personal care, but home health nurses are required to perform patient assessments and treatments, such as intravenous therapy or tube or ostomy care. One of the biggest challenges to the provision of care by these agencies is the ability to achieve adequate staffing of trained caregivers, especially in rural areas, due to workforce shortages. In some instances, the area Administration on Aging can be a resource at the local and county level for locating available services.

Physician visits in the home are possible in some areas, but these services are not common. Typically, transportation must still be arranged to access physician care in an office or clinic. An alternative to this may be home visits by advance practice nurses, such as nurse practitioners, who can extend the service range of the physician and can change medication therapy orders.

In this setting, access to both prescription and over-the-counter (OTC) medications is generally through community pharmacies or mail-order pharmacies. Home health agencies generally do not include consultant pharmacist services to provide drug regimen review, medication therapy interventions, or collaborative drug therapy management services; however, entrepreneurial pharmacists have created unique practices of this nature in some outpatient settings.

Physical therapy, occupational therapy, speech therapy, or clinical laboratory services can also be arranged in the home setting.
Adjuncts and Alternatives to Home-Based Care

When an individual’s lifelong home is not practical, options such as senior housing or life care communities present alternatives to placement in an institutional setting. Senior housing is often just a high-rise or campus of apartments, condominiums, or garden homes that cater to the needs of older individuals. Such settings may offer housekeeping, laundry services, security, maintenance, fitness centers, and social activities. Some may also provide transportation services or even have an on-site clinic with access to nursing staff. Continuous care retirement communities, sometimes called life care communities, are based on the concept of “aging in place.” They provide a continuum of private apartments, assisted living apartments, skilled nursing units, and long-term care units all in one campus-style location. Individuals buy a residence in the community but also pay a monthly fee. For this investment, a community resident can move between any level of care as needed, based on health status, while still paying the same or similar monthly fee regardless of the extent of daily care required.

For individuals who cannot be left alone but do not have a 24-hour caregiver, or for those whose primary caregivers/family members must work outside the home, adult day centers can provide a solution that allows individuals to continue to live in their own home while providing socialization, supervision, or assistance during the day. Daytime meals, assistance with daily activities, or medication administration is often available.

A PACE (Program of All-Inclusive Care for the Elderly) program is an optional benefit under Medicare or Medicaid for individuals frail enough to be eligible for long-term care. In states that offer this benefit, the program bundles services in a comprehensive package that can be delivered at home or in adult day centers. As of 2013, there were 98 PACE programs in 31 states. PACE medical teams usually include primary care physicians; nurses; physical, occupational, and recreational therapists; social workers; personal care attendants; dietitians; and drivers. The services must include all Medicare and Medicaid services provided by that state, but typical services may include personal care; respite care; physical, occupational, speech, or recreational therapy; meal provision; social work; medication ordering; and coordination of dental, optometry, podiatry, hospital, and long-term care. Enrollees pay a premium each month, and PACE receives a fixed monthly reimbursement from Medicare and Medicaid.

Assisted Living Facilities

Individuals who require additional assistance with daily activities but who do not require the 24-hour care of a LTCF may be candidates for an ALF. These environments are similar to senior housing but usually provide more structured services. In addition to those previously described, these settings usually provide all meals, on-site nursing services, medication administration assistance, and assistance with some ADLs. Although residents of an ALF may require some assistance with daily activities, they must be able to remain safely unsupervised within their apartment and have at least some mobility (e.g., transferring from bed to chair to commode). Residents may require adaptive equipment or assistive devices, but they must be able to accomplish these tasks under their own power.

Whereas an ALF provides more formal services, it is not regulated in the same way as long-term care. The LTCF requirements for frequency of physician follow-up, drug regimen review by a pharmacist, or specific patient assessment and monitoring by nursing staff are not mandated in the ALF setting at the federal level. This setting is regulated at the state level, so requirements may be more or less stringent based on location.

Long-Term Care Facilities

Individuals requiring the highest level of care may require long-term care placement. Long-term care may also be the only option for persons who do not require the highest level of care but for
whom proper caregiving resources in their own home are not available or affordable. These environments provide 24-hour care, and strict state regulations under the Department of Health and Human Services govern the day-to-day operations of licensed facilities. Facilities that receive reimbursement from Medicaid or Medicare must also comply with federal regulations under the Centers for Medicare & Medicaid Services. These regulations govern staffing requirements, the frequency of physician follow-up, and the frequency and scope of consultant pharmacist activities. The facility operations manual and interpretive guidelines provide specific requirements for medication documentation, administration, monitoring, storage, labeling, and security.

Medicaid is the largest payer for long-term care, and facilities that receive reimbursement under Medicaid must dedicate a proportion of their facility beds to the care of individuals who qualify for Medicaid based on income. Facility residents must expend available resources, in a process commonly termed spending down, until they qualify for Medicaid.

Generally, SNFs receive reimbursement from Medicare. Medicare does not pay for long-term residential care but will provide reimbursement for short-term rehabilitation or other specialized care as a transitional step after hospital discharge. Medicare requirements for regular monitoring of patient progress and updating of the plan of care often presents one of the most reliable mechanisms for the interprofessional team to interact. Although pharmacists are not providers under Medicare, the consultant pharmacist to a skilled facility or unit will often participate in these team deliberations as part of a service contract with the facility.

An alternative to the traditional long-term care setting is a Green House. This is a small facility that is home to up to 10 residents, with a 24-hour universal worker, called a shabaz, who attends to daily needs. The concept is based on the Eden Alternative, in which the environment is home-like, centered around the individual, and is intended to allow “aging in place” with a small group of residents and staff with whom close relationships can be formed. The Green House project began in 2005, and in just the past few years has grown from 20 Green Houses in 16 states to hundreds of Green Houses either open or in development in over 30 states. Depending on the location, the facilities vary in whether they are licensed as long-term care facilities or SNFs and, therefore, whether reimbursement is available from Medicaid or Medicare. Mechanisms for arranging formal healthcare services and regulations mandating the frequency of follow-up will also depend on licensure status.

Long-Term Acute Care, Emergency Departments, and Hospital Environments

One type of hospital environment often associated with older patients is long-term acute care, although this environment is not exclusive to patients over age 65 years. This type of hospital is associated with longer average lengths of stay than a traditional hospital environment (at least 25 days) and provides treatment for chronic diseases to medically complex patients. Some of the typical needs in this environment include ventilator weaning, wound care, post-stroke care, long-term infectious disease management, or other care that is more medically complex than that provided in a nursing home environment.

In the acute care environment, some hospitals have specialized Acute Care for Elders (ACE) units that are dedicated to special geriatric needs. The care in these environments includes a prepared environment, early rehabilitation, frequent medical review, and early discharge planning in a patient-centered and function-focused approach designed to prevent hospital-associated functional decline. Meta-analyses of studies evaluating outcomes of ACE unit care indicate that hospitals employing these components of care are associated with fewer falls, less delirium and functional decline, shorter hospital stay, and lower costs.

In most acute-care environments, elderly patients are cared for as part of the general adult population, and the majority of hospitals and
emergency departments do not have specialized units or care teams for geriatric patients. Therefore, all staff members need to be aware of the special needs of frail patients in order to provide optimal care and avoid iatrogenic problems. This includes, in part, an understanding of age-related changes in physiology that affect risk of disease, cause atypical clinical presentation, and alter medication response. Subsequent chapters will describe the principles of geriatric assessment, age-related changes in pharmacokinetics or dynamics, and an organ-system approach to pathophysiology and pharmaceutical care.

It is also worth mentioning the specific aspects of the care environment that are not always conducive to an elderly patient's needs. Consider the care that is taken to prevent loss of a patient's personal effects on admission to the emergency department. Personal clothing, glasses, hearing aids, dentures, and other belongings are usually removed, bagged, and labeled. Patients are provided with a hospital garment. Although in most cases a patient may not need to be physically restrained, the placement of intravenous lines or catheters essentially restrict the patient to the bed. It is isolating and confusing for most individuals to feel, in addition to the effects of the illness or injury that caused the admission, being cold, and unable to see, hear, speak, or ambulate well. These processes are expedient and perhaps necessary given the specific circumstance, but consider the coping abilities of an individual in this circumstance with an underlying cognitive impairment, or in a patient who is at risk for mental status change or delirium due to his or her illness. If agitation results, either in the emergency department or in the hospital unit, elderly hospitalized patients are vulnerable to the prescribing of chemical restraints, an intervention which may be crucial for the delivery of safe care in cases where the patient presents a danger to self or others but which can be problematic if not used judiciously.

Elderly patients are also particularly vulnerable to the effects of immobility associated with hospitalization. Thromboembolism and infection are two of the most significant adverse outcomes thought to be related to immobility, but pressure ulcers, worsening pain, constipation, increased vulnerability to orthostasis, deconditioning and muscle weakness, functional decline, and falls are common. Medication therapy can directly or indirectly exacerbate the risk of each of these. Finally, elderly patients are vulnerable to iatrogenic harm caused by preventable adverse drug events.

**The Continuum of Care**

**Challenges for Seniors Moving from One Care Venue to Another**

The three most significant barriers to the assurance of good care are availability, cost, and coordination. The demographics of the geriatric population and the lack of healthcare workforce have already been discussed. The availability of assisted living apartments or long-term care beds is also inadequate to meet population demands. The costs associated with specialized services can also be prohibitive for individuals on a fixed income, despite health benefits, especially if savings are depleted by costs associated with chronic disease care. The cost of long-term care can vary significantly from state to state, but in 2010 the average cost was estimated to be $205 per day ($6,235 per month) for a semi-private room and $229 per day ($6,965 per month) for a private room. The cost for a one-bedroom unit in an ALF environment was $3,293 per month. In the home, costs associated with a home health aide were $21 per hour, and $67 per day for adult day healthcare center services. In addition to cost, access to geriatrics-trained caregivers can be difficult.

Medicare benefits provide coverage for hospital or physician office visits and up to 100 days (per illness) of skilled nursing care after hospitalization under Parts A and B, and a prescription drug benefit under Part D, but Medicare does not pay for assisted living or long-term care. Medicaid does provide long-term care benefits to individuals who qualify based on income, but the biggest challenge is the availability of Medicaid beds in many LTCFs,
where there may be extensive waiting lists. Unfortunately, for this reason, selecting a long-term care environment often becomes less a matter of choice than of the first-available spot. In the home-based care environment, there are a variety of mechanisms for funding various services, but these are inconsistent from state to state in terms of who is eligible and what services are covered.

In addition to availability and cost considerations, another risk for elderly patients is moving from one care venue to another. Pharmacists are familiar with the concept of polypharmacy. The premise is that the more medications on the regimen, the more complex the pharmacological reactions between compounds and disease states, increasing the vulnerability to cost, medication error, interactions, adverse reactions, morbidity, or even mortality. A similar concept in geriatric healthcare is polyvenuism. The more an older patient, who may already be frail due to multiple comorbidities or functional deficits, is shuttled between healthcare settings and healthcare providers, the higher the risk of miscommunication, gaps in information, medical or medication errors, and adverse outcomes.

Current standards require healthcare institutions to employ safe medical practices, and most employ some method of medication reconciliation on admission or discharge. However, there is no requirement that each distinct environment employ uniform methods of carrying this out. Each healthcare environment will employ its own system of documentation and clinical records maintenance. Therefore, the same safeguards that exist within a healthcare environment may not exist between healthcare environments. The ability to optimize transitions of care has become a major factor affecting reimbursement for hospital systems.

After returning to an outpatient environment, geriatric patients face challenges in receiving streamlined care. Coordinating the care provided by all of the care vendors is challenging. From physicians’ offices (including primary care physicians, their mid-level practitioners, and any number of specialists), to home visits by nurses, therapists, or other caretakers, to the community pharmacy, individuals not only receive care from multiple venues, but the documentation of that care is maintained in separate records sources. If a home health agency is involved, it may be possible to compile most relevant health information into a comprehensive medical record, as medical history data, treatment orders, medication orders, therapy orders, assessment data, and laboratory monitoring are generally ordered or at least coordinated through the same agency. By contrast, an independent individual who coordinates his or her own healthcare and receives services in an a la carte fashion would be the sole source of complete healthcare information, regardless of what data are maintained by each health professional involved in his or her care. It must be recognized that in either of the above scenarios, pharmacists are still “external vendors,” as home health agencies do not have their own pharmacies and could not mandate use of a particular pharmacy even if they did.

A patient will have the freedom of choice in pharmacy services, and he or she may use more than one pharmacy. Therefore, it is important to remember that the medication lists maintained by other health professionals or by a home health agency are merely reflective of the current intent for medication orders, and specific (and repeated) “brown bag” medication and adherence review is often necessary to ascertain whether such medication list accurately mirrors what the patient is actually filling and taking. In such a review, the pharmacist would collect all available pill bottles, containers of OTC products or supplements, and other materials related to medication taking or medication monitoring that the patient could provide and compile a complete medication history along with an assessment of patient adherence, level of understanding or
health literacy, and assessment of medication outcomes.

**Access to Medication/Pharmacy Services**

An individual's access to prescription and OTC medications is usually through community or mail-order pharmacies throughout most of the continuum of care. Therefore, it is the community pharmacist who has perhaps the greatest opportunity for interaction with geriatric patients. In home-based care, senior housing, and assisted living, individuals will retain their choice of pharmacy provider(s). This is also true in long-term care. Although LTCFs with skilled nursing units will contract with a specific pharmacy vendor to provide medications under Medicare Part A, individuals receiving residential care may still choose from any pharmacy provider that will supply medications to a LTCF. The major difference, of course, between these settings has more to do with who controls medication acquisition, administration, and monitoring: the patient or a caregiver.

Independent, community-dwelling individuals are responsible for their own medication purchases, refills, adherence, technique, self-monitoring, and self-reporting of outcome. The primary means of identifying efficacy outcomes or adverse drug reactions is through patient self-report. This means that there must be a mechanism for one or more health professionals to interact with patients on a regular basis to perform specific evaluations of medication therapy. The importance of medication review is widely accepted, and most health professionals perform this to some degree during their interactions with all patients. However, it could be argued that there are barriers to the optimal performance of this task, and that recognizing and overcoming these barriers could help with adverse drug outcomes in elderly populations.

For instance, a thorough medication review should have the appropriate time dedicated to evaluating all indications, drugs, doses, intervals, durations, interactions, contraindications, adverse effects, efficacy endpoints, cost, and adherence. This activity also must include all OTC products or supplements. Time should also be spent in ensuring that the patient understands the purpose of each medication, what to expect and how to monitor, and how to administer, especially for those medications requiring special technique. This often requires more time than can be afforded during a physician office visit or a home care nurse visit. In addition, the frequency of patient encounters can vary. Some patients may see their doctor once a year or less, and in such situations the data from even a very thorough medication review can quickly become outdated.

Pharmacists can provide medication review and can bring a high level of expertise in drug therapy to this task, but there are also barriers to optimal review for these health professionals as well. In the community setting, pharmacists may have limited data. Pharmacy databases are limited to the history of prescriptions filled or refilled within that pharmacy or pharmacy chain, or at least to those prescriptions filled under that individual's prescription drug plan. Also, these databases do not contain full medical history information. Although history taking or basic patient assessment by the pharmacist can elicit some pertinent information related to indications for each medication and efficacy or side effect outcomes, these activities are often hindered by time constraints or the reliability of patient report.

In settings where medication assistance or medication administration is provided by a nurse or nurse's aide, patients may or may not be aware of what medications they take or why or how they should be administered and are vulnerable to medication error by the health professional. In these settings, such as in long-term care, a consultant pharmacist has access to the medical record and a more thorough evaluation of drug therapy outcomes may be possible, but such individuals often do not have the ability to intervene prospectively, at the time of prescription processing. A consultant pharmacist can periodically oversee a staff member passing medications and make recommendations about
proper administration but is usually not going to be able to do so before the first dose is administered. Periodic drug regimen review can also identify medication-related problems, but this is usually limited to the identification of problems associated with medications for which administration has already commenced, and in some cases, such as with antibiotics, the course of medication therapy may be initiated and completed in between chart reviews, making the ability to intervene in the case of inappropriate drug, dose, interval, route, duration, or monitoring very difficult.

By contrast, inpatient settings usually have on-site pharmacies that supply medications to patients during the time they are on the healthcare facility's service. In these environments, the same department that has the prescription processing responsibility also has the access to the complete medical record, perhaps making drug therapy intervention for medication-related problems easier for all patients in that environment, not just older patients. Increasingly, pharmacy departments are staffed to provide pharmacist participation in both the pharmacy operations and medical team deliberations in the hospital units, but this is contingent on whether an institution recognizes their importance and provides adequate allowances for budget and time to accommodate these services.

Two types of pharmacy services are available in the long-term care setting. Long-term care pharmacies provide prescription processing, unit-dose packing, and delivery of products to LTCFs and skilled facilities, or LTCFs with skilled units can also contract with such pharmacies to provide medications to their residents under Medicare Part A. However, LTCFs cannot mandate the choice of pharmacy to residential-stay individuals, where choice of pharmacy vendor, much like the choice of personal physician, is a resident's right. That means that while a long-term care pharmacy may provide medications to all Part A recipients, it may not be the pharmacy vendor for all facility residents.

The other type of pharmacy service in long-term care is consultant pharmacy, and in this setting this type of service is mandated by state and federal regulation. Consultant pharmacists must perform a drug regimen review for every resident of a LTCF every 30 days and submit recommendations about drug therapy problems to the director of nursing or the medical director. These recommendations do not have to be accepted and implemented; however, they do have to be acted on, meaning that a recommendation or request must be answered with either an “agree” or “disagree,” and a rationale should be provided if the prescriber feels that implementing the change is not appropriate. Consultants will also advise the facility about appropriate procedures for medication ordering, labeling, storage, security (particularly for controlled substances), administration, monitoring, and record keeping.

Therefore, in addition to review of the medical records, consultants will periodically audit these processes by inspecting medication rooms and medication carts, observing the nursing staff pass medications, implementing controlled substance inventory counts, and reconciling and destroying expired or discontinued medications. Consultant pharmacists also often participate in facility oversight activities, such as medical director's meetings or quality assurance monitoring.

Prescription processing services and drug costs are reimbursed via direct consumer payment or through prescription drug plans, including Medicare Part D, and medication regimen review and patient counseling is an expected part of this. However, based on the above discussion it is clear that additional pharmaceutical care is often necessary beyond this, in the home, in the clinic, or within the interprofessional team. Such services are not formally reimbursed by Medicare, Medicaid, or most third-party insurance plans. Most pharmacist services of this nature are provided on a fee-for-service basis through independently negotiated contracts between the pharmacist (or pharmacy) and the institution. Because long-term care is mandated to retain the services of
A consultant pharmacist, these institutions will set aside a portion of their budgets for the provision of this service. In ALFs or other care venues, contracting for pharmacist services is voluntary in most states. In light of the significant challenges associated with adverse drug outcomes in the geriatric population, it is important to critically evaluate the potential cost savings of additional pharmaceutical care interventions in the various healthcare environments so as to determine how to design, provide, and budget for services of this nature.

Summary of Pharmacy Services

Whether the site of practice is the community pharmacy, the long-term care pharmacy, a hospital, a clinic, an interprofessional team, or a consultant practice, the pharmacist provides vital input and expertise in a few key areas:

- Drug regimen review and identification of medication-related problems
- Drug therapy interventions to prevent or resolve medication-related problems
- Assessment of medication history or medication administration
- Assurance of continued drug therapy monitoring for safety and efficacy
- Advice about proper storage, handling, and disposal of drug products
- Drug information and education

Pharmacist Contributions to the Healthcare Team

There is a long way to go to improve the quality chasm described by the IOM in our current healthcare system. Older patients, especially those with complex medical histories, are vulnerable to the fragmentation of care that often results from healthcare that is delivered across multiple venues by multiple individuals with varying levels of geriatric expertise. The IOM proposes the ability to work in interdisciplinary teams as one of five core competencies essential to meet the needs of the 21st century healthcare system. The IOM states that “all health professionals should be educated to deliver patient-centered care as members of an interdisciplinary team, emphasizing evidence-based practice, quality improvement approaches, and informatics,” but the specific role of pharmacists in this team is currently being defined. There is a compelling need for pharmacists with geriatrics training to be a part of the emerging landscape of team care. However, the hope for reforms tomorrow does not help the patient seen in practice today. At this time, whether a formal team exists or not, there is no substitute for the health professional who is knowledgeable about where the current system is broken to recognize how his or her patients are likely to be vulnerable and to advocate or intervene on their behalf. In addition to understanding the age-related changes in physiology that affect pharmacokinetics, pharmacodynamics, and quality of drug outcomes, today’s pharmacists must be familiar with the logistical barriers to pharmaceutical care such as polyvenuism; inconsistent, incomplete, or out-of-date medical records data; and asynchronous communication with other health professionals. Skill sets included not only knowledge of pathophysiology and drug therapy, but the ability to audit, investigate, reconcile, or verify patient history or medication data and to facilitate communication, education, and recommendations to patients and their caregivers about drug therapy concerns.

**KEY POINT:** Health professionals who understand the potential areas of vulnerability for older patients in the healthcare system are in a better position to advocate for their patients.

Caregiver Burden

**Who Is a Caregiver?**

A caregiver is an individual who assists with or performs functions for another who cannot perform tasks independently. These tasks could be anything from assistance with home
maintenance, meal preparation, transportation, or finances, all the way to personal care, such as personal hygiene/grooming, dressing, eating, or ambulating. Based on such a definition, almost all of us may find ourselves in the role of caregiver in some way during our lives. In healthcare, the definition of a caregiver is often divided into formal and informal categories. Formal caregivers are individuals who provide their services professionally, for a fee. Nurses and nurse’s aides in the long-term care, assisted living, or home healthcare industries usually come to mind when most people think of this group of caregivers, and it is often assumed that formal caregivers have training as healthcare professionals. However, professional caregivers are often hired in the role of sitter or personal companion, and there is no specific training requirement to fulfill such a role. Informal caregiving is more often taken on by family members, and in some instances by a friend or volunteer. Whereas the American Red Cross can serve as a resource to provide basic training for informal caregivers, this is voluntary and based on availability. Informal caregivers are not paid for their time and must balance caregiving responsibilities with other work or family commitments. In fact, the majority of adults who receive long-term care at home receive almost all of their care from unpaid family and friends.

**Caregiver and Care-Recipient Characteristics**

It is estimated that 28.5% of the U.S. population over the age of 18 (approximately 65.7 million caregivers in 31.2% of U.S. households) serves as a caregiver in some capacity for relatives or friends. The majority of caregivers provide care to adult recipients, with 70% caring for an individual over age 50, and the average age of the care recipient has increased in the last 5 years from 66.5 to 69.3. One third of caregivers provide care to two or more people. Sixty-six percent of caregivers are female, of an average age of 48, providing an average of 20 hours or more per week in the caregiver role. One in four of these caregivers reports that the person he or she cares for has Alzheimer disease or other cognitive impairment, and the number of care recipients reported as requiring prescription medications has increased to 93%.

**What Is Caregiver Burden?**

Caregiver burden is the caregiver’s appraisal of the balance between care demands, resources, and the quality of the caregiver/care-recipient relationship and may be a better predictor of the use of formal healthcare services than measures of the care recipient’s mental or physical health or functional abilities. The two types of burden are those that affect personal decisions or activities, and those that affect the relationship between the caregiver and the care-recipient. There are also several levels of burden based on the intensity of caregiving activities required. These levels range from Level 1, where caregivers perform no help with ADLs and spend only a few hours per week in caregiving activities, up to Level 5, where caregivers assist with at least two ADLs and provide care more than 40 hours per week.

Caregiver burden has a significant impact on both the physical and emotional health of the individual providing care. After controlling for age, gender, education, and other factors, there is a relationship between the level of care provided and the impact caregiving has on the caregivers’ perceived health. Higher caregiver burden levels also correlate with higher rates of unaddressed patient needs.

There has also been a *widower effect*, described as a consequence of caregiver burden. A large study of married couples demonstrated the effect of hospitalization or death of one spouse on the health of another. After an individual is hospitalized, his or her spouse’s risk of death increases and remains elevated for up to 2 years, with the greatest risk occurring within 30 days of the partner’s hospitalization or death. During this initial 30 days, hospitalization of a spouse confers just as much risk of dying as the death of a spouse.
Measuring Caregiver Burden

One of the most common instruments to quantify caregiver burden is the Zarit Index. This instrument evaluates strain by assessing time to self, feelings of stress or anger, strained relations with others, lack of privacy, effects on personal health, impedance on personal life, and loss of control or choice. It also assesses whether caregivers feel guilt over not doing enough, or not knowing how best to provide care.\textsuperscript{35}

Other instruments include the Caregiver Strain Index, Caregiver Burden Inventory, Caregiver's Burden Scale in End-of-Life Care, the Screen for Caregiver Burden, and the Caregiver Activity Survey.\textsuperscript{36-40} They vary in their assessment of time; behavioral, physical, social, and emotional factors; as well as in the specific population of caregivers/care recipients tested. There are a number of ways these tools are useful in quantifying caregiver burden. First, a tool that allows recognition of caregivers at risk for poor outcomes as a result of significant burden can facilitate coordination of resources. In addition, assessments of caregiver burden have been employed in clinical trials evaluating the efficacy of interventions for frail elderly patients. For instance, the Resource Utilization in Dementia scale was included among the battery of tests administered in the evaluation of memantine for Alzheimer disease.\textsuperscript{41} Finally, the ability to accurately quantify caregiver burden may have implications for public policy, especially as it relates to funding for elder care services. This is perhaps the most challenging aspect of caregiver burden assessment. Even scales that evaluate cost of care via estimates of time lost from wage earning employment or value of informal services provided do not completely quantify the total cost associated with informal care. This is a critical area that warrants further research due to the significant need to reduce the strain associated with informal caregiving.

Caregiver Resources and Strategies to Alleviate Caregiver Burden

Of the resources currently available to caregivers, most home and community-based services programs are administered via State Units on Aging, with Area Agencies on Aging being the most common.\textsuperscript{19} State programs use a variety of methods to track healthcare expenditures for the various services provided; therefore, no uniform method exists to assess costs nationwide. In general, funding for state programs comes from the National Family Caregiver Support Program, Medicaid waivers, the state's general funds, and individual contributions from recipients.

The most common service provided, available in all 50 states, is respite to family members.\textsuperscript{42} However, there is significant variability in the scope of services available from state to state. Some of the most common services available include in-home respite, adult day services, or overnight respite care in a facility.\textsuperscript{33} Differing eligibility requirements, service complexity, and fragmentation of services (even within a single state) have been cited as the most significant barriers to coordinating caregiver support. In addition, it is difficult to pinpoint how well state programs meet the needs of the populations they serve. Those programs that employ formal assessment typically direct the evaluation at the care recipient, but fewer than half of states report assessing needs of family caregivers.\textsuperscript{42}

KEY POINT: A significant amount of the care for older individuals is provided by informal caregivers. Although resources are available to informal caregivers, they are not uniform across the country, and there is not always a reliable mechanism for coordination or communication between formal and informal care.

Caregivers are essential keys to coordinating seamless care for frail patients. They are gatekeepers of information, coordinators of schedules, supervisors of treatment regimens, and often the voice of the patient. When there are gaps in documentation, they often know the history that is not found in the clinical record.
When the clinician is struggling to determine whether a clinical presentation represents a significant change from a patient's baseline status, caregivers know the day-to-day norm. They can provide the personal details that remind us their loved one is an individual and not just a patient case. It is a position of power and vulnerability at the same time, as the caregivers themselves are vulnerable to stress, fatigue, and poor health outcomes. Health professionals need to seek their input when evaluating a frail patient and designing a care plan, not only to ensure that the patient's needs are met, but to do so in a way that is appropriate based on the caregiver's abilities and needs.
CASE 1: USE OF A SUBGROUP PERSPECTIVE TO APPROACH LITERATURE

Setting:
Outpatient geriatric assessment clinic.

Subjective:
A 95-year-old white female, ES, is brought to a clinic by a family caregiver for a routine visit.

Past Medical History:
Hyperlipidemia, history of TIA, mild Alzheimer disease, osteoarthritis.

Medications:
Donepezil 10 mg hs, aspirin 81 mg daily, acetaminophen 325 mg two tablets four times daily, multivitamin daily.

Allergies:
No known drug allergies.

Social History:
ES is widowed, lives with daughter in daughter’s home.

Family History:
Noncontributory.

Objective:
Physical exam unremarkable, vitals: BP 148/84 mmHg, P 82 BPM, RR 20, T 97.8°F
Lipid panel: TC 154 mg/dL, LDL 102 mg/dL, HDL 42 mg/dL

Assessment:
The medical resident wishes to aggressively treat ES’s cholesterol. He cites reduced risk of cardiovascular outcomes, such as stroke, with the attainment of a goal LDL value of <100 per the PROVE IT trial. Is this evidence being appropriately applied to this patient?

Plan:
To answer the question posed in this case, it must be determined whether the adult treatment principles should be extrapolated to ES. The PROVE IT trial is a widely cited clinical trial, but does its finding apply to all geriatric patients? The first step in answering this question is to identify whether there is an evidence base of primary literature with a specific focus on subgroups of patients similar to the patient in this case. In any literature identified, the study’s objective and design, its inclusion and exclusion criteria, as well as the baseline characteristics of enrolled subjects should be examined to determine how similar they are to the patient. This includes an evaluation of what age strata are represented, whether both sexes are represented, and whether similar characteristics, such as comorbidity levels, living/treatment environments, or functional or cognitive status, are represented. Even if these characteristics are included, it should be evaluated whether they are represented in large enough numbers to allow subgroup analysis. In this particular case, the study focus does not mirror the clinical situation of the patient. In age strata or medical history, the population in the clinical trial cited does not optimally represent the case patient, suggesting that a choice about drug therapy selection or target outcome made for her based on this study is not optimally evidence-based.
Rationale:
The question posed in ES’s case is actually less about whether to treat her hyperlipidemia (see Chapter 7), but it does ask whether clinical literature from the general adult population applies to her. Scrutiny of the baseline characteristics and inclusion or exclusion criteria are steps in ascertaining whether the data were derived from a population representative of an individual patient, or if a more tailored literature search is required.

Case Summary:
When the evidence is limited, choices about initiation of drug therapy will often become a judgment call, simply because an evidence-based treatment decision cannot be made for a patient who is not represented in the evidence base. The case of ES illustrates only one disease state for which the clinician must question whether conclusions drawn from a study in the adult treatment realm are the best course of action for this elderly patient.
CASE 2: COORDINATION OF CARE ACROSS MULTIPLE VENUES AND CAREGIVERS

Setting:
Private home of a community-dwelling individual.

Subjective:
An 88-year-old African American man, LH, has just had two new prescriptions for ophthalmic eye drops presented to the pharmacist in a community pharmacy by a neighbor. LH has called on his friend to do this errand for him because he cannot drive because of poor vision. The friend declines medication counseling by the pharmacist stating “these aren’t for me anyway” and reports that LH has a home health nurse that visits each week and can help him.

Past Medical History:
Hypertension, hyperlipidemia, history of myocardial infarction 2003, and glaucoma.

Medications:
Enalapril 10 mg twice daily, metoprolol 50 mg twice daily, pravastatin 40 mg at bedtime, aspirin 162 mg daily, timolol 0.25% solution, 1 drop each eye twice daily, latanoprost 0.005% solution, 1 drop each eye at bedtime (eye drops prescribed by ophthalmologist, not primary care physician).

Allergies:
Penicillin.

Social History:
LH lives alone, no close family.

Family History:
Not known.

Objective:
Physical exam not performed; last recorded vitals from a blood pressure check in the pharmacy include BP of 110/60 and pulse of 54 BPM.

Assessment:
LH is receiving both formal and informal assistance from more than one venue or caregiver, and there are multiple ways in which LH is vulnerable to a suboptimal outcome:

1. At the pharmacy: The pharmacist filling the prescription has likely performed a drug regimen review and has offered counsel, but this has been declined.
2. By home health: The home health nurse who visits once weekly would not be able to directly assist with daily administration of the drops or other daily medications.
3. By the prescriber: The prescriptions have been prescribed by an ophthalmologist, not the patient’s regular doctor.

Plan:
To prevent a medication-related problem, LH must be assessed for opportunities to coordinate care. In optimal circumstances, communication would occur not only between the pharmacist and LH or his caregiver but also between the pharmacist and the home health agency and physicians involved. Each health professional has data or information that the others do not. The pharmacist could provide medication counseling to the home health nurse and can provide updated information about the current medication list and refills to the primary care doctor. The
home health nurse can reinforce drug information about administration and self-monitoring to LH, perform weekly vitals assessments, and regularly ascertain medication understanding and enquire about adherence.

Rationale:

1. Coordination of care is necessary because this patient is vulnerable to potentially preventable adverse outcomes. In the pharmacy setting, even if medication counseling had been provided it would have to have been relayed through LH’s friend. Although the provision of written prescription information is required, LH’s poor vision may hinder the utility of this method of instruction. This is especially problematic due to the nature of the prescriptions that were filled.

2. Ophthalmic drops require specific technique for proper instillation, and the administration of two eye drops requires that adequate time be allowed in between drops, for optimal absorption. Although the systemic effect of an ophthalmologic beta blocker preparation is likely small, LH is already receiving an oral beta blocker and has had blood pressure and heart rate at the lower end of the desired range. Therefore, changes to these parameters should be monitored. The home health nurse will not be able to administer these medications for him but perhaps could provide education and evaluate weekly vitals, especially if there were communication from the pharmacist to alert the nurse why this was needed. In order to do this, there must be a mechanism for the pharmacist to ascertain which home health agency is providing care.

3. With the dispensing of these two new prescriptions, the pharmacist would now have a more up-to-date medication list than would be available to the primary care physician. By contrast, the pharmacist has no direct access to the medical record with a complete medical history, so although the pharmacist likely performed a drug–drug interaction check against the prescription history in the pharmacy database, the completeness of this check may be limited, because the pharmacist may not be aware whether there are other medications that have been prescribed and filled elsewhere. The office of the primary care physician would maintain records about medical history and prescriptions ordered by that doctor but would not be aware of any potential interactions with the new medications from other providers until LH returns to the office and provides a complete medication history, which may not occur until after he experiences a problem.

Case Summary:

Each health professional performs one aspect of the care of LH, but all the parts do not equal a whole unless they are knitted together. Without coordination, LH is vulnerable to subtherapeutic effect of the ophthalmic medications if not administered properly or potential exacerbation of bradycardia if continuous monitoring of vitals is not ensured while on both his antihypertensive regimen and his eye drops. There is no way for each member of the healthcare team to be aware that a potential problem exists unless they are communicating. In traditional practices, the biggest barrier is a lack of a habitual or comfortable mechanism for each caregiver to communicate with one another.

Is the relationship between pharmacist and doctor one that would facilitate notifications about updates or changes or concerns with drug therapy, either by phone or by fax? Does the home health agency maintain contact information for the patient’s pharmacy of choice so as to have access to the pharmacist when drug therapy questions arise? If so, is such contact regularly made? Is the workflow in the pharmacy conducive to the performance of pharmaceutical care activities such as telephoning LH and offering verbal counsel, or offering to coordinate counsel with the home health nurse if LH is hard of hearing or would like a hands-on demonstration of medication administration? For each answer of “no” to these questions, there is perhaps a hole in the safety net that is intended to knit LH’s care services together.
Clinical Pearls

Hospital Documentation Versus Long-Term Care Facility Documentation

- On transfer between the hospital and long-term care, the hospital’s history and physical or discharge summary is often used as the admission history and physical in the LTCF. Regulations allow this, provided the document is authenticated as accurate and current by the resident’s physician. However, it may not always be complete. Nursing facility regulations require that all medications, acute or chronic, must have a supporting indication for use, but hospital documentation may often be limited in scope to the primary medical conditions/medications pertinent to the inpatient admission, and the hospital’s medication reconciliation may not always include data about medication indication or the rationale behind medication changes. Understanding that it can take up to 6 weeks to observe an adverse outcome resulting from a change in drug therapy made in the hospital, it is likely that many patients have been discharged to another care venue, such as a skilled nursing facility or LTCF, before such a problem is realized. Therefore, decisions about medication continuation/discontinuation or duration of therapy are perhaps some of the most critical at the time of transfer, yet this decision making is often hampered by lack of complete data.

Formulary Management

- Formularies are common strategies to control costs and to standardize medication interventions for various clinical scenarios. These strategies work best in healthcare facilities where (1) there is a single pharmacy vendor, (2) there is one (or very few) third-party payer(s), or (3) prescribers’ clinical privileges are bound to the policies and procedures of the institution. The hospital setting is an example where a single formulary may apply, but in most other settings, such as long-term care, there is no single vendor for medical or pharmacy services, so any number of formularies could be dictating choice of medication within the facility’s population. Formularies may change with each transition as a patient moves from the hospital to skilled care to long-term care. For consultant pharmacists in long-term care, it is often difficult to know exactly which medications are on which formularies as these transitions occur. Therefore, it may be valuable for the consultant to record contact information for each individual patient’s pharmacy vendor. In the event that questions arise about which product to recommend as part of a drug therapy intervention, the consultant could ascertain the appropriate options through that route.
Chapter Summary

Based on what we know about the heterogeneity of the geriatric population, it is easy to understand why a healthcare workforce must include a strong group of professionals well-versed in the needs of this population. This introductory chapter has outlined not only the diversity of the geriatric population but also the available workforce, care venues, services, and programs. Subsequent chapters will provide further information regarding the social, financial, physiological, and psychological vulnerabilities of this population, but the pertinent message of this chapter is that a thin and fragmented care and support network fundamentally exacerbates such vulnerabilities. Healthcare professionals who understand the cracks and deficits in our current health system may be in a better position to advocate for their patients. Recognizing different populations of elderly patients and using a subgroup perspective in the approach to the clinical literature allows for clinical decision making that is more tailored. Recognizing the type and availability of healthcare services, including the healthcare professionals who are providing them, can assist with the development of services to better meet the population’s needs. On behalf of the geriatric population of today, as well as the future population (of which each of us may one day count ourselves a member), healthcare professionals must rise to meet the challenges described in this text.

Self-Assessment Questions

1. A healthcare diagnostics company has conducted a study of a new home machine that will allow patients who take warfarin to test and monitor their international normalized ratio (INR) at home. The study demonstrated that regular home monitoring reduced the incidence of adverse events related to supratherapeutic INRs. What subgroups of elderly patients may present the greatest concern in applying these data?

2. An ALF offers a medication reminder service that entails assistance with the set-up of pill boxes and a daily visit by a nurse’s aide who will remind patients to take each dose and assess adherence via pill count. This individual can also take blood pressure and heart rate prior to the administration of any medication, if required. What medications would most likely be administered safely with the use of such a service?

3. A 42-year-old woman who works outside the home and has school-aged children has recently taken her mother into her home after hospitalization for hip fracture. Her mother has mild dementia and is currently mobile at a wheelchair level only. She requires supervision and assistance with ADLs, and she is eligible for Medicaid. What resources are most widely available to caregivers in this type of situation?

References


Ethical and Socioeconomic Considerations

Susan W. Miller

Learning Objectives

1. Apply the tenets of biomedical ethics to ethical dilemmas commonly encountered in providing pharmaceutical care to geriatric patients.
2. Explain issues related to communication in the care of the geriatric patient, including informed consent, privacy and confidentiality, and surrogate decision making.
3. Describe patient, caregiver, family, and legal issues associated with end-of-life decisions.
4. Explain the effects of socioeconomic issues on access to pharmacy care by geriatric patients.
5. Describe medication financing options (including affordable medications) available for geriatric patients.

Key Terms and Definitions

Autonomy: Respect for autonomy obliges healthcare professionals to honor the choices of adults with decision-making capacity, allows for a patient’s right to self-determination, avoids paternalism, allows for the acceptance of the free choice of the patient, and ultimately permits the patient to make final decisions relating to his or her healthcare.

Beneficence: Beneficence obliges healthcare professionals to help others and promote their welfare.

Boxed Warning: A notice in the prescribing information of a prescription medication that alerts prescribers and patients of severe or fatal side effects of the medication; often added retrospectively following identification of side effects in the routine use of the medication. This was previously known as a “black box” warning.

Culture: The group to which one belongs; extends beyond race and ethnicity to include age, gender, religion, and health beliefs.

DNR: Do not resuscitate; an order that states cardiopulmonary resuscitation (CPR) is not to be performed in the event of cardiac or respiratory arrest.

Ethnogeriatrics: Healthcare for geriatric patients from diverse populations.
Introduction

Ethical and socioeconomic considerations are integral components in the delivery of healthcare to geriatric patients. Often, the care of a geriatric patient centers on important decisions regarding healthcare choices and end-of-life issues for those who lack the mental capacity or physical ability to effectively communicate their personal choices. Access to healthcare, healthcare disparities, and financing healthcare are vital socioeconomic issues for older citizens. This chapter will describe ethical issues and socioeconomic considerations related to geriatric patients.

Ethics and Biomedical Ethics

Biomedical ethics is the branch of ethics concerned with the life of the patient, and at the core of biomedical ethics are issues regarding the protection of life. Table 2-1 provides examples of many important biomedical issues. The promise to adhere to the principles of biomedical ethics is contained in the various oaths affirmed by healthcare professionals, including pharmacists. Of the various tenets of biomedical ethics, four are particularly applicable in geriatric pharmacy practice: respect for patient autonomy, nonmaleficence, beneficence, and justice. Ethical dilemmas arise when these tenets are in conflict, and a choice between two “rights” must be made. Biomedical ethics often involves situational ethics, in which a particular clinical condition may cause both patient and caregiver values to evolve in order to cope with changing circumstances. Ethical dilemmas are often encountered during geriatric patient care because treatment options are rarely straightforward.

Pharmacists are obligated to apply the tenets of biomedical ethics when providing pharmaceutical care for geriatric patients. For example, by providing full disclosure regarding the risk-benefit profile of medications, thus allowing the patient to make a personal choice as to whether to consume a particular medication, the pharmacist is providing patient care as well as respecting autonomy and acting with beneficence and nonmaleficence. The use of medications with a boxed warning in the prescribing information can be a particularly difficult ethical dilemma for the pharmacist providing care for geriatric patients. Recently approved drugs may be more likely to have unrecognized adverse drug reactions (ADRs) than established drugs, especially in older frail patients. Serious ADRs commonly emerge after FDA approval, and the safety of new agents cannot be known with certainty until a drug has been on the market for several years. Yet, physi-
 Pharmacists often prescribe new pharmacotherapeutic agents with the promise of improved efficacy and ease of dosing compared to older agents. For example, the use of thiazolidinediones can be problematic in the geriatric diabetic patient. The thiazolidinediones can cause or exacerbate congestive heart failure and contain a boxed warning in the prescribing information about this effect. Pharmacists have an ethical responsibility to inform patients of these potential effects and suggest the use of alternative oral antidiabetic agents that may be more appropriate and have fewer adverse effects in their specific situation. However, it is difficult for the community pharmacist who may lack detailed information about the patient’s history, physical findings, and laboratory results to know when the risk outweighs the benefit for an individual patient. Thus, an ethical dilemma must be resolved.

Another example involves the use of atypical antipsychotic agents, such as risperidone, ziprasidone, and quetiapine, that are often prescribed off label to manage behaviors in elderly patients with dementia. Their use is associated with increased mortality in elderly patients with dementia-related psychosis, mostly due to cardiovascular events or infectious diseases. The prescribing information for atypical antipsychotic agents contains this information in a boxed warning. Pharmacists have the ethical responsibility to provide complete drug information to patients and/or surrogate decision makers regarding potential nonpharmacologic and alternative pharmacotherapeutic options for behavior management. This particular situation is fraught with ethical issues, as the patient with dementia may have difficulty providing input for his or her preferences, nursing home staff and family are frequently frustrated with behavior problems, and busy physicians may not adequately evaluate all components driving the behaviors. An additional example involves the use of the oral anticoagulant dabigatran to manage patients with nonvalvular atrial fibrillation. Postmarketing reports of bleeding with dabigatran were at a higher rate than reported in the FDA approval process, and this adverse event presents a challenge in medication management because of the lack of an available reversal agent for the anticoagulant effects and the continued need for an agent to manage the atrial fibrillation. The ideal scenario is for the pharmacist to participate in patient assessment meetings with other healthcare providers, including patients and surrogate decision makers, and having each participant explain the problems objectively and discuss potential solutions. These interprofessional interactions result in a carefully chosen treatment plan devised with consideration of the risks and benefits to the patient.

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Pharmacists practicing as consultants for institutionalized geriatric residents of skilled nursing facilities have a responsibility to make recommendations to add, modify, or discontinue pharmacotherapies in these patients following evidence-based medicine, disease management practice guidelines, algorithms, or sound clinical judgment. The pharmacist should strive for a balance between beneficence and nonmaleficence in adhering to practice guidelines and making recommendations regarding drug therapy. Prior to the pharmacist making a recommendation to prescribe an antihyperlipidemic agent, such as a statin, for prevention and/or management of hypercholesterolemia in a specific geriatric patient, the life expectancy, effectiveness of therapy, adverse effects, and time to benefit should be taken into consideration. At issue is the general lack of high-quality evidence to use in assessing the risks and benefits in patients over the age of 80 years for most practice guidelines.

When the needs of two individuals in similar circumstances are unequal, the obligation is to treat them in a fair manner and to act with justice. This means that those who have a greater need may rightly receive more of a particular resource than those with less need. Pharmacists who immunize patients should follow the guidelines for administration of these vaccines. During the vaccination period prior to influenza season, pharmacists should apply the tenet of justice to provide protection for the most susceptible patients and prevent vaccine shortages. Justice, when applied to resource allocation in the provision of healthcare, is central to the debate over the rationing of healthcare and whether healthcare is a right or a privilege.

**Principles of Ethical Decision Making**

Three principles of thinking that frame ethical decision making and are applicable in the patient care setting have been described by Kidder: ends-based thinking, rules-based thinking, and care-based thinking. Ends-based thinking follows the maxim “Do whatever produces the greatest good for the greatest number.” Decisions regarding the allocation of pharmacotherapy resources, as in cost-benefit analysis, are often rooted in ends-based thinking. Practical examples of ends-based thinking include implementation of therapeutic substitution within a formulary and the use of tiered copays in pharmacy benefit programs. Administration of influenza vaccine in all institutionalized patients will provide the best protection for that population against the disease. However, some patients may object or may be allergic to components of the vaccine, causing a fallacy in this line of thinking.

Rules-based thinking follows the maxim “Stick to your principles (the rules) and let the consequences follow.” Decisions involving the obligation that the pharmacist owes to the patient follow rules-based thinking. An example of rules-based thinking is the provision of complete factual drug information to patients during counseling, including the most severe, albeit rare, adverse effects of the medication. This counseling would include boxed warnings.

Finally, care-based thinking follows the maxim “Do unto others as you would have them do unto you.” The pharmacist’s feeling of empathy for the patient is the result of care-based thinking. Examples of care-based thinking in the practice of pharmacy include providing drug information to patients receiving sample medications or whose insurance plan requires them to obtain their medications from mail-order pharmacies. The pharmacist who does not charge for this information will also not see a profit from sales of a prescription.

**Respecting Choices**

In the process of providing healthcare and pharmaceutical care to the geriatric patient, multiple opportunities exist for making choices relative to this care. Choices regarding the types of care necessitate full disclosure of the risks and benefits of each type; choices regarding privacy
and confidentiality affect the delivery of care and personal health information; a patient’s culture can affect his or her healthcare beliefs and choices; and caregivers and family may take part in the shared responsibilities of the decision making. The tenets of biomedical ethics can be applied to the resolution of dilemmas that are central to the provision of healthcare for geriatric patients. The dependent nature of many geriatric patients can complicate the issues, as the older patient may require assistance in making choices relative to healthcare. As a result of cognitive impairment or communication disorders, geriatric patients are often unable to express a preference for their healthcare matters. Publicized cases involving ethical issues have provided guidance for patients, family, and healthcare providers in the areas of establishing patient preference regarding healthcare decision making and the right to die. These cases have dealt with issues related to the persistent vegetative state, physician-assisted suicide, and an individual patient's request for the right to die.

Communication between the pharmacist and the older patient is an additional factor involved in resolving ethical dilemmas and respecting healthcare choices of geriatric patients. Communicating with older patients can be especially challenging, secondary to extensive medical histories, multiple medications, and physiologic barriers that may complicate the interaction. Pharmacists should practice compassionate communication with geriatric patients and their caregivers and should treat patients with dignity and respect, regardless of the cognitive or physical condition of the patient. Accommodations should be made for patients with hearing or visual impairments, such as speaking slowly and clearly, maintaining eye contact, and using visual aids written in a large type font and/or pictures and diagrams. A reassuring and supportive attitude while communicating can make the older patient feel comfortable in sharing his or her healthcare choices.

**Informed Consent**

Autonomy on the part of the geriatric patient and respect for autonomy on behalf of the pharmacist are manifest in the precept of informed consent. Informed consent has replaced paternalism in the decision-making processes of healthcare and allows the patient to make final decisions regarding healthcare choices only after receiving full disclosure regarding the risks and benefits of the available options.

The seven elements of informed consent that must be met for the patient to make a proper decision regarding healthcare choices are competence (to understand and decide), voluntariness (in deciding), disclosure (of material information), recommendation (of a plan), assurance of understanding, decision (in favor of a plan), and authorization (of the chosen plan).

A basic meaning of competence is the ability of the patient to perform a task, which in the realm of healthcare is to understand the decision at hand. Comatose patients and those with significant cognitive or psychological impairments lack competence and are unable to provide informed consent. This is especially an issue with delirium, where a patient’s ability to understand may fluctuate. Furthermore, medications may cloud a patient’s mentation, creating further difficulties. Voluntariness must be present and must not be affected by coercion or manipulation by healthcare professionals or relatives, or by medications or psychological disorders. Confusion can prevail when multiple family members disagree on the best choice for a patient, and the patient is unable or unwilling to oppose a choice which differs from his or her own perspective. Various cultures may involve family members or healthcare professionals to a greater or lesser degree in helping the patient make his or her own decision, and these differences must be evaluated to ensure coercion is not present. Disclosure of information must be appropriate, based on contemporary professional standards, and must be what a reasonable person would expect to be told in a similar situation. Recommendation of a plan must be based on the best information.
obtainable. **Assurance of patient understanding** must be determined by the healthcare provider. Understanding may be difficult to measure, and the circumstances in which the information is disclosed may affect the patient's understanding. If a patient has poor health literacy, information must be disclosed in a manner he or she can understand. To assess comprehension, the clinician should have the patient explain what he or she understands about the choices. Furthermore, in an emergency situation where time is of the essence, if the patient is emotionally distraught, or if medical terms are not clearly described, misunderstanding may occur. When all of the elements of informed consent are met, the patient has the right to make an autonomous decision, and the decision should be respected by healthcare professionals. Finally, **authorization** for any procedure must occur through a signature on a legally valid document.¹¹

Informed consent is most frequently associated with participation in clinical research; however, written informed consent for nursing home residents with dementia treated with psychoactive agents is mandated in some states and may become commonplace.¹² Nearly one-third of elderly nursing home residents with dementia are receiving an antipsychotic medication, and those with impaired decision-making ability are 50% more likely to receive these medications. The combination of high utilization and patients with dementia makes the process of informed consent in this situation precarious.¹³

**Privacy and Confidentiality**

The Health Information Portability and Accountability Act of 1996, also known as the Privacy Rule or HIPAA, provides federal protections for personal health information (PHI) held by covered entities (healthcare providers and healthcare institutions) and gives patients certain rights regarding the information.¹⁴ A patient's understanding of his or her personal health record and how PHI is used allows the patient to assume responsibility for the accuracy and authorization of use of PHI. The basic rights under HIPAA are:

- Request a restriction on certain uses and disclosures of PHI
- On request, obtain a paper copy of the notice of information practices
- Inspect and/or receive a copy of personal health record
- Request an amendment or correction to personal health record
- Obtain an accounting of disclosure of PHI
- Request for communication of PHI by alternative means or at alternative locations
- Revoke authorization to use or disclose PHI except to the extent that action has been taken

Application of HIPAA policies in the healthcare setting ensures that geriatric patients have the right to receive care in privacy. This means that in the community pharmacy setting, medication counseling should be provided in a private area, away from other patients; in the nursing home, patients should receive their care, such as the administration of medications, in their room and not in the public areas of the facility. Pharmacy examples of HIPAA violations include the selling of prescription information to companies tracking prescribing patterns of physicians or the unauthorized speaking with family members regarding a geriatric patient's medications.

**KEY POINT:** Pharmacists have the obligation to ensure that PHI is only disclosed as patients permit.

**Ethnogeriatrics: Cultural Considerations**

It is the professional responsibility of healthcare providers to become knowledgeable regarding the cultures of the patients they serve and to understand the implications of these cultural beliefs on individual health behaviors. There are data to show that lack of cultural competence on the part of the healthcare provider can lead to
disparities in healthcare access and provision. Information is available for pharmacists to determine and further develop their personal cultural competence. Cultural considerations are important in understanding the health beliefs of patients from various generations, backgrounds, religions, and traditions. Cultural competence on the part of healthcare providers ensures that the effects of factors such as socioeconomic status, education, race/racism, ethnicity, culture, sex, disability, and sexual orientation are considered when providing care related to the health and functioning of the older population.

The term ethnogeriatrics was first established by the Stanford Geriatric Education Center in 1987 and serves to recognize the challenges of caring for a growing, ethnically diverse, aging population. The ETHNIC(S) mnemonic is a tool for clinicians to use for cultural evaluation during a patient encounter. Each letter in the mnemonic stands for a cultural aspect of care involved in a patient encounter and should allow the healthcare provider to appreciate the centrality of culture in illness: Explanation, Treatment, Healers, Negotiate, Intervention, Collaboration, and Spirituality. Table 2-2 provides questions to be asked during the patient encounter. Pharmacists are encouraged to incorporate this model into their patient encounters when providing pharmaceutical care such as counseling on medications, medication therapy management, and medication reconciliation for geriatric patients. The use of assessments such as the ETHNIC(S) tool should help healthcare professionals recognize the heterogeneity of older minority patients, avoid stereotyping and generalizations, and help to provide culturally competent pharmaceutical care.

Medication adherence in the elderly is affected by one’s attitude toward self-efficacy (the belief that one can perform a specific behavior under differing conditions), medication-efficacy, confidence in the prescribers’ knowledge, perceptions about natural products and home remedies, beliefs of control (over one’s health), and illness perceptions. Intergenerational relationships and the importance of traditional familial hierarchies influence health-related behaviors and decision making in the Southeast Asian, Japanese, and Hispanic cultures. Elders from Southeast Asian cultures base their beliefs on healthcare and medicine in the ancient practice of Chinese medicine. They characterize Western medicine as stronger, faster, and curative compared to their folk medicines as weaker, slower, yet preventive. This belief system may explain why patients from Southeastern Asian cultures may choose to be noncompliant with medications by taking lower doses.

Members of Native American cultures believe in the interconnectedness of healing, spiritual beliefs, and community and look to modern medicine to alleviate modern ills such as hypertension and diabetes. They look to traditional Native American remedies to cure common problems such as pain or a “sick spirit” (defined as mental illness and/or alcoholism). Older Japanese Americans respect healthcare practitioners as authoritarian figures, place a high level of trust in them, and tend to allow healthcare practitioners to make treatment-related decisions for them. Members of the African American culture are more likely to express negative and suspicious beliefs about physicians’ advice on medical treatments, including the prescribing of drugs, and report spiritual beliefs that God is ultimately responsible for health. Patients with a faith-based lifestyle can perceive use of medications as a sign of disbelief or weakness. It is important for pharmacists to understand their patients’ cultural beliefs so that medication counseling can be tailored, taking these beliefs into consideration.

What one thinks of illness and how it develops (i.e., the result of unhealthy habits, random occurrence, accidents, or punishment) and one’s views on care (i.e., professional, self-care, do nothing) and treatments (i.e., holistic, scientific based, “natural” remedies) can all affect medication adherence. The Greatest Generation or traditionalists may be noncompliant with pain medications as a result of stoicism. They may delay getting refills or may not complete a course of antibiotics as a result of hoarding
(saving for a rainy day) or may be more dependent on home remedies as a result of self-reliance. The Baby Boomer generation is composed of a post–World War II cohort who expect a prescription to be written at every patient encounter. At the other end of the spectrum, a younger group, the Woodstock Generation, rely on natural products for cures. Baby Boomers are interested in information related to their medications and generally accept patient counseling. The use of alternative medicine, including dietary supplements and herbal remedies, is increasing in all age groups and has doubled among geriatric patients since the year 2000.22 Pharmacists should enquire about the use of alternative therapies when taking a medication history and when providing patient counseling regarding prescription medications. In counseling geriatric patients, pharmacists should be prepared to discuss alternative therapies and make recommendations when asked.

Table 2-2. ETHNIC(S): A Framework for Culturally Appropriate Geriatric Care17

<table>
<thead>
<tr>
<th>Cultural Aspect</th>
<th>Direct Question or Statement to Be Asked or Stated (Use the Patient’s Phraseology)</th>
<th>Probe Questions to Be Asked or Actions to Be Taken</th>
</tr>
</thead>
<tbody>
<tr>
<td>Explanation</td>
<td>Why do you think you have this symptom/illness/condition?</td>
<td>What do friends, family, and others say about these symptoms? Do you know anyone else who has had or who has this kind of problem? Have you heard about/read/seen it on television/radio/newspaper/Internet? (If the patient cannot offer an explanation, ask what concerns him or her about the problems.)</td>
</tr>
<tr>
<td>Treatment</td>
<td>What have you tried for this symptom/illness/condition?</td>
<td>What kind of medicines, home remedies, or other treatments have you tried for this illness? Is there anything you eat, drink, or do (or avoid) on a regular basis to stay healthy? Tell me about it. What kind of treatments are you seeking from me?</td>
</tr>
<tr>
<td>Healers</td>
<td>Who else have you sought help from for this symptom/illness/condition?</td>
<td>Have you sought help from alternative or folk healers, friends, or other people who are not doctors for help with your problems?</td>
</tr>
<tr>
<td>Negotiation</td>
<td>How best do you think I can help you?</td>
<td>Try to find options that will be mutually acceptable to you and your patient and that incorporates your patient’s beliefs rather than contradicting them.</td>
</tr>
<tr>
<td>Intervention</td>
<td>This is what I think needs to be done now.</td>
<td>Determine an intervention (e.g., diagnostic, pharmacological, psychosocial, educational) with your patient that may also incorporate alternative treatments, spirituality, healers, and other cultural practices (e.g., foods eaten or avoided in general and when sick).</td>
</tr>
<tr>
<td>Collaboration</td>
<td>How can we work together on this, and with whom else?</td>
<td>Collaborate with the family, family members, healers, and community resources.</td>
</tr>
<tr>
<td>Spirituality</td>
<td>What role does faith/religion/spirituality play in helping you with this symptom/illness/condition?</td>
<td>Tell me about your spiritual life. How can your spiritual beliefs help you with this?</td>
</tr>
</tbody>
</table>

**KEY POINT:** Patients often have cultural beliefs that symptoms or side effects are just part of growing older and cannot be relieved. These beliefs may influence medication adherence.
The previous paragraphs illustrate cultural characteristics that have been documented in the literature as being associated with specific populations. Although this information is helpful in working with patients who identify as members of a population, the clinician must not ignore that individual patients do not always ascribe to a population’s collective cultural norm. One resource that may be helpful in describing and applying cultural competent care to geriatric patients is the iGeriatrics smartphone application from the American Geriatrics Society. It includes a Geriatrics Cultural Navigator that contains information about 15 different ethnic groups and practice pearls on how to apply the information to recognize variations in an individual from group stereotypes.

**Shared Decision Making**

Geriatric patients have the right to autonomy in decision making, but, in reality, geriatric patients often participate in shared decision making that involves healthcare providers, family, and caregivers. As described above, various cultures approach healthcare decision making as shared between the individual and one or more of these groups. However, the patient, if capable, must make his or her own informed choice. Pharmacists must be aware of cultures where strong extended family bonds or paternalism may overshadow an individual’s right to make his or her own decisions. A patient has the best opportunity to maintain autonomy when working with an interprofessional team.

**Religious and Spiritual Influences**

Religious and spiritual beliefs and practices influence many patients’ attitudes toward health and wellness, and the older patient is no exception. Religion has been noted as being very important to a majority of Americans age 50 and older.24 Religion and spirituality are important coping mechanisms in the presence of illness and therapy. Religion is defined as an organized system of beliefs, practices, and symbols designed to facilitate closeness to a higher power and includes the understanding of one’s relationship with and responsibility to others.25 The three Abrahamic monotheistic religions, Judaism, Christianity, and Islam, have carefully considered positions on medical ethics, and devotees to these religions often turn to religious leaders for guidance in biomedical ethical decision making.26 Spirituality is defined as the quest for understanding life’s ultimate questions and the meaning and purpose of living, which often leads to the development of rituals and a shared religious community.24 Religious and spiritual beliefs can help patients cope with illness and may aid in incorporating health changes into their lives. An older patient’s religion and/or spirituality can influence their decision making in aspects of healthcare and his or her approach to accepting the recommended course of care. Healthcare providers should enquire about and acknowledge the religious and spiritual beliefs of their patients when making patient care decisions. Healthcare providers may not share the same religion and/or spirituality as their patients, and this may cause misunderstanding or conflict between the healthcare provider and the patient.26

**Surrogate Decision Making and Advance Directives**

A surrogate decision maker is an agent who acts on behalf of a patient who lacks the capacity to participate in a particular decision.1 According to the Patient Self-Determination Act of 1991, healthcare organizations, including hospitals and nursing homes, that receive Medicaid and Medicare funds have the responsibility to explain to patients, staff, and families (through written information) that patients have a legal right to direct their medical and nursing care as it corresponds to existing state laws. This federal regulation requires healthcare organization personnel to enquire of all adults admitted as inpatients whether they have an advance directive (AD) for healthcare and to inform patients of their right to refuse treatment.
The three primary purposes of the Patient Self-Determination Act are:

- to educate the public about state laws governing the refusal, withholding, and withdrawal of treatment at the end of life;
- to encourage wider use of ADs to prevent the uncertainty among doctors and family members that often leads to prolonged treatment of the dying, and in some cases to lengthy court battles; and
- to reduce the costs of treatment at the end of life by reducing unwanted and unnecessary intervention and the perceived need for defensive medicine.\(^{27,28}\)

All states have regulations concerning ADs, although their legal requirements may vary. ADs are specific instructions, prepared beforehand, that are intended to direct a person’s medical care if he or she becomes unable to do so in the future. They allow patients to make their own decisions and preserve some measure of control regarding the medical care they would prefer to receive if they develop a terminal illness or a life-threatening injury (e.g., Alzheimer disease, cerebrovascular accident, severe head injury). ADs can also designate a surrogate to make decisions about medical care if the patient becomes unable to make or communicate those decisions. ADs can avoid costly or specialized interventions that a patient may not desire, reduce personal worry and futile feelings of helplessness or guilt for family members, reduce overall healthcare costs, and minimize legal concerns for those involved. Individuals are advised to keep a copy of the AD with their personal papers and provide copies to their healthcare providers, family, and proxy.\(^{29}\)

The living will and the durable power of attorney for healthcare are types of ADs important to the care of geriatric patients.\(^{29}\) A living will may indicate specific care or treatments the individual consents to or refuses under certain conditions. Care, treatments, or procedures may include CPR in the event of cardiac or respiratory failure, “do not resuscitate” (DNR) designations, artificial nutrition (intravenous or tube feedings), prolonged maintenance on a ventilator, antibiotic therapy, blood transfusions, spinal taps, blood cultures, initiation of dialysis, organ donation, and autopsy. A durable power of attorney for healthcare is a legal document that allows an individual to appoint a proxy to make medical or healthcare decisions in the event the individual becomes unable to make or communicate such decisions personally. The durable power of attorney for healthcare does not allow the proxy to make legal or financial decisions for the individual. In an effort to simplify the health-related decision-making processes at the end of life, states and organizations are combining ADs into a single document described as an actionable medical order that can accompany a geriatric patient as he or she transitions between and among levels of care. One such example is the MOLST (Medical Orders for Life-Sustaining Treatment) document utilized in several states. Another popular form to document AD is the Five Wishes™ form, which is recognized as a valid legal document in 42 states and is available in 26 languages.\(^{30}\)

**Problems with Advance Directives**

Problems with ADs include confronting a patient in distress with a list of possible procedures and requiring the individual to make decisions under duress. This can lead to unnecessary anxiety and poor decision making on the part of the patient. Other criticisms are that the language in ADs can be vague or nonspecific, and an individual’s preferences may change with circumstances. Individuals should be counseled to discuss their healthcare issues with healthcare providers, family, and caregivers and complete ADs while they are in a state of good health. An alternative time to complete ADs is during the preadmission process to a healthcare institution, prior to a planned medical procedure. A patient executing an AD should have the ability to make decisions for him- or herself based on the information and choices presented, weighing the information to determine what the decision will mean on a personal level and then communi-
cating that decision via the AD. If a person is unable to follow this process, he or she is said to lack mental capacity.

A person may lack mental capacity due to an intellectual disability, dementia, brain injury, or mental illness. This lack of mental capacity may be temporary. Legal capacity and the rights that go with it remain in effect until death, unless a court of law determines that a person can no longer manage personal affairs in his or her own best interest and court intervention is necessary to protect the person. Healthcare practitioners, even if they think the person is incapable of making a decision, cannot overrule the person’s expressed wishes unless a court declares the person legally incapacitated. Guardianship is a legal mechanism by which the court declares a person incompetent and appoints a guardian. The court transfers the responsibility for managing financial affairs, living arrangements, and medical care decisions to the guardian.\(^1\)

Surveys of elderly African Americans, whites, and Hispanics regarding attitudes toward completion of ADs have revealed that African Americans and Hispanics were less likely than white patients to have appointed a healthcare proxy or completed an AD. The differences in AD prevalence were related to knowledge of healthcare proxies, availability of a potential healthcare agent, beliefs about the necessity of a formally appointed proxy in the presence of involved family, experience with life-prolonging technologies, age, and self-perceived health status. These findings highlight the need for healthcare providers to be sensitive to cultural differences while avoiding stereotyping patients and their beliefs around healthcare choices based on race and ethnicity.\(^31\) Surrogate decision makers, such as a healthcare proxy or guardian, can benefit emotionally from the patient having ADs in effect.

Patients, however, are fully capable of making and communicating end-of-life decisions as they approach the end of their life. These patients are faced with choices that are based on their current experience, as opposed to the hypothetical situations covered by ADs. For patients facing these dilemmas, end-of-life decisions are based on the expectation for their length of life weighed against their quality of life. Length of life decisions are based on the probability that death is highly likely and further efforts to postpone it are not likely to succeed. Quality-of-life decisions address the value or worth of life if the patient survives.

**Life-Sustaining Treatments**

Life-sustaining treatment is directed primarily at preserving life despite disease, rather than at curing the disease. The use of ventilators, feeding tubes, dialysis, and CPR are considered life-sustaining treatments, while chemotherapy is a treatment often directed at curing disease. Artificial nutrition via gastric feeding tubes or intravenous feedings is considered a life-sustaining treatment but is usually classified as a medical intervention instead of routine nursing care or comfort care.\(^32\) After several court decisions regarding feeding tube issues, the American Medical Association changed its code of ethics on comas to allow physicians to ethically withhold food, water, and medical treatment from patients in irreversible comas or persistent vegetative states with no hope of recovery, even if death is not imminent.\(^33\) Issues surrounding life-sustaining treatments are commonly in litigation, and these laws will continue to be written.

**DNR Orders**

When the decision is made not to revive a patient in the event of a cardiac or pulmonary arrest, a DNR order should be requested. It may be written for a patient by the physician upon consultation with the patient (if possible), the family, or the proxy. The DNR order must be in writing and must be signed and dated by the physician. Patients and their families should be provided information regarding a DNR as it relates to the
clinical situation, so that an informed decision can be made. Often, the cultural and spiritual beliefs of a patient and family guide the decision. However, the DNR document must be on file at the patient’s current venue and cannot be transferred from site to site. For example, a DNR signed and filed at a nursing home is not in effect at the hospital where the resident may be transferred for treatment.

**Assisted Suicide**

Assisted suicide, also known as legal-assisted suicide or physician-assisted suicide, is the act of ending one’s own life with the help of another person (i.e., a physician). Most states have laws specifically prohibiting assisted suicide, but in the recent past a few states have legalized assisted suicide, which allows physicians to prescribe a fatal dose of medication to a patient whom the physician feels is likely to die within 6 months. Proponents of assisted suicide argue that persons should have the right to control their own destiny, including the right to control how and when they die. Opponents of assisted suicide point to the principle of nonmaleficence, arguing that taking a life is harmful by definition. Pharmacists may be involved in ethical dilemmas if requested to dispense prescriptions for medications to be used in assisted suicide.

**Withholding and Withdrawing Treatments**

Withholding treatment is a decision to forego initiation of treatment or medical interventions for a patient. When death is imminent and cannot be prevented by available means, it is morally permissible to withhold treatment that can yield only a precarious prolongation of a life that may involve a great burden for the patient or family. Withdrawing (or discontinuing) treatment should be considered when the patient is in a terminal condition and there is a reasonable expectation of imminent death, when the patient is in a noncognitive state with no reasonable possibility of regaining cognitive function, and/or when restoration of cardiac function will last for a brief period. Futility of treatment, as it relates to medical care, occurs when the healthcare practitioner recognizes that the effect of treatment will be of no benefit to the patient. Morally, the healthcare provider has a duty to inform the patient there is little likelihood of success. The determination as to the futility of a type of medical care is a scientific decision made by the physician. Withdrawal of treatments may be selective; treatments to provide comfort could be continued while therapeutic treatments are discontinued.

Although there is ample evidence to assist in the prescribing of safe and effective doses of medications, there is little evidence regarding when or how to stop or discontinue these same medications. Holmes et al. have proposed four criteria to consider when adding or removing medications from a geriatric patient’s medication regimen:

1. The patient’s remaining life expectancy (based on actuarial charts and modified by the patient’s current health status and history)
2. The time required to obtain benefit from the medication (i.e., immediate for analgesics compared to months or years for antihyperlipidemic agents)
3. The goals of care (a balance among prevention, treatment, and palliation)
4. The treatment targets (relief of specific symptoms that agree with goals of care)

**Palliative Care**

Palliative care has evolved from total care of the terminally ill patient to active and comprehensive medical care aimed at symptom relief from chronic illness. Palliative care is specialized medical care with a focus on identifying and relieving pain and other symptoms of serious illness. The goal of palliative care is to improve quality of life for seriously ill patients at any stage of illness, not solely terminal illness.

**Hospice**

Hospice is an interprofessional program of palliative care to give supportive care to the dying
patient and his or her family in the final phase of a terminal illness. The focus of the care is on comfort and quality of life rather than cure. The goal is to enable the patient to be comfortable and free of pain, so that he or she lives each day as fully as possible, and to this end aggressive methods of pain control (including high doses of analgesics) may be used. The philosophy of hospice is to provide multidisciplinary support for the patient's emotional, social, and spiritual needs as well as medical symptoms as part of treating the whole person. Hospice is currently funded by Medicare for patients who are deemed to have a life expectancy of less than 6 months by their physician. A patient may choose to enroll in a hospice program if he or she meets this requirement. Hospice programs are available in the home or in freestanding facilities, nursing homes, or hospitals. Specific laws allow for dispensing opioid analgesics with fewer restrictions in hospice patients. Frequently, hospice patients require medications in specially compounded formulations to ease medication administration. Pharmacists may be involved in interprofessional discussions to optimize palliative therapies and to minimize treatments aimed at prolonging life in hospice patients. Chapter 6 provides more information on palliative and hospice care for the geriatric patient.

Abuse, Neglect, and Safety Issues in the Elderly

Placement Issues

Aging creates losses of health, financial resources, loved ones, and independence. Assisting geriatric patients in compensating for losses may involve a change in the living situation to ensure safety and to allow for access to the necessary healthcare. Alternatives for living situations for older patients include high-rise independent living communities, assisted living communities, life care retirement communities, skilled nursing facilities, and nursing homes/long-term care facilities. Each of these situations provides a specific type of care, and planning in anticipation of a change in functional status can ensure the best environment for the patient's needs. Social issues that complicate illness in the geriatric patient include family and caregiver burnout, changes in family dynamics related to the illness, family guilt, patient reluctance or refusal to change the living situation, availability of the appropriate type of living situation, and financing for healthcare. As in the case of ADs, planning for potential living situations usually allows for more informed choices and smoother transitions.

Abuse and Neglect of the Elderly

If the social issues described above that complicate geriatric care are not adequately addressed, the geriatric patient can become vulnerable to the environment and experience poor outcomes. Elder abuse is classified as a type of domestic violence and is defined as any intentional, unintentional, or negligent act or series of acts that cause harm or serious risk of harm to a vulnerable person, typically 60 years of age or older. The acts of abuse may be passive or active, and the abuser may not be aware of the consequences of his or her actions. Elder abuse may be classified as physical, emotional, financial, or sexual and may involve neglect, abandonment, or any combination of these. Elder abuse can occur in the home, in the community, or in healthcare institutions. Screening tools are available for use by healthcare professionals to detect such abuse. Misuse of medications, such as oversedation or underuse of analgesic agents in a patient with chronic pain, is a form of physical abuse. In providing pharmaceutical care to geriatric patients, pharmacists should evaluate medication regimens, the frequency of refill requests, as well as the physical status of the patient to screen for possible abuse and medication misuse. Pharmacists, as well as all healthcare professionals, are responsible for reporting elder abuse to local or state authorities (i.e., Adult Protective Services, police, or institutional administrators).

Decisions for People in Nursing Homes

Patients are often admitted to nursing homes because they are dependent on the services
of others. Most nursing home residents suffer from some degree of physical impairment, many suffer from cognitive impairment, and for all the ability to provide self-care is limited. Decision making for residents of nursing homes often involves ethical issues, and if residents of nursing facilities have ADs in place or a named proxy, the decision-making process related to healthcare issues is less problematic.\textsuperscript{38}

The Nursing Home Resident’s Bill of Rights was incorporated into the 1987 Nursing Home Reform Law in order to ensure residents maintained the same rights as individuals living in the community. An emphasis on the resident’s dignity and right to self-determination pervades the law, and facilities that receive Medicare or Medicaid funds are obligated to meet its requirements. The overall goal is to prevent a decline in health or quality of life as a consequence of care provided by a facility. A long-term care ombudsman program is established to aid a resident or surrogate decision maker if these rights are not honored. Common ethical issues encountered in the nursing home and their association to the Nursing Home Bill of Rights is summarized in Table 2-3.\textsuperscript{39}

**Socioeconomic Considerations**

The economic and social conditions under which people live determine their health. Diseases are primarily determined by a network of interacting exposures that increase or decrease the risk for disease. The terms *health disparities* or *healthcare inequality* refer to the differences in the quality of health status, health outcomes, and the access to healthcare across groups of people.\textsuperscript{40} Health disparities result from three primary factors:

1. the characteristics (personal, socioeconomic, and environmental) of groups;
2. the barriers encountered by groups trying to enter the healthcare delivery system; and
3. the quality of care received by groups.

Geriatric patients can experience healthcare disparities as a result of the above factors. Specifically, geriatric patients can experience problems accessing healthcare through:

- lack of insurance coverage (more likely to delay medical care and go without prescription medications, more likely be without health insurance or prescription insurance);
- lack of a regular source of care (more likely to avoid routine healthcare and receive fragmented care through emergency rooms or clinics);
- lack of financial resources to pay for healthcare;
- structural barriers (poor transportation, inability to schedule appointments quickly or conveniently, long wait times for care);
- healthcare financing system (likely to be enrolled in plans with limited coverage or with limited choices of healthcare providers);
- health literacy (problems obtaining, processing, and understanding basic health information; this may lead to a poor understanding of when to seek care for symptoms); and
- age (fixed incomes make paying for healthcare difficult, impaired mobility or lack of transportation makes accessing healthcare challenging, inability to use the Internet as a source of information regarding healthcare and wellness).\textsuperscript{41}

**KEY POINT:** An important healthcare disparity for geriatric patients is access to affordable prescriptions, which affects medication adherence and leads to poor healthcare outcomes.

Pharmacists have a professional obligation to assist geriatric patients in overcoming the socioeconomic barriers that result in healthcare
<table>
<thead>
<tr>
<th><strong>Nursing Home Residents Have the Right to:</strong></th>
<th><strong>Examples</strong></th>
</tr>
</thead>
</table>
| Be fully informed                           | Available services and the charges for each service  
Facility rules and regulations, including resident rights  
Address and phone number of ombudsman and state survey agency  
State survey reports and the facility plan of correction  
Advance plans of a change in rooms or roommates  
Assistance if a sensory impairment exists  
Information provided in a language you understand |
| Complain                                   | To present grievances to staff or others, without fear of reprisal and with prompt efforts to resolve the grievances  
To contact the ombudsman program  
To file a complaint with the state survey agency and certification agency |
| Participate in care                        | Receive adequate and appropriate care  
Be informed of all changes in medical condition  
Participate in own assessment, care planning, treatment, and discharge  
Refuse medication, treatments, and physical and chemical restraints  
Review own medical record  
Be free from charge for services covered by Medicaid or Medicare |
| Privacy and confidentiality               | Facilitating private and unrestricted communication with any person of their choice  
During treatment and care of one’s personal needs  
Regarding medical, personal, or financial affairs |
| Security during transfers and discharges   | Remain in facility unless removal is necessary to meet the resident’s welfare, the health/safety of others is at risk, or for lack of payment for services  
Require 30 days’ notice and includes right of appeal  
Incorporate sufficient notice for preparation  
Ensure safe transfer or discharge with sufficient preparation by facility |
| Dignity, respect, and freedom             | To be treated with consideration, respect, and dignity  
To be free from mental/physical abuse, corporal punishment, involuntary seclusion, and physical/chemical restraints  
To exercise self-determination  
To have security of possessions |
| Visits                                     | By a resident’s personal physician and representatives from the state survey agency and ombudsman programs  
By relatives, friends, and others of the resident’s choosing  
By organizations or individuals providing health, social, legal, or other services  
Residents have the right to refuse visitors |
| Make independent choices                  | Make personal decisions, such as what to wear and how to spend free time  
Ensure reasonable accommodation of one’s needs and preferences  
Choose a physician and a pharmacy  
Participate in community activities, both inside and outside the facility  
Organize and participate in a resident council  
Manage one’s own financial affairs |
disparities by providing medication counseling and healthcare information that is readily understandable by geriatric patients and assisting these same patients in obtaining the most affordable medications. The newer pharmaceutical care practice models of medication therapy management and medication reconciliation are valuable in ensuring that geriatric patients receive the maximum benefit from their medications, particularly during transitions between and among care settings.

**Financing Healthcare**

Healthcare in the United States is financed through a combination of health insurance programs and out-of-pocket expenses by patients. Many changes have occurred in health insurance plans since their introduction in the early 1900s, and currently over 83% of healthcare expenditures are paid by private or public insurance programs (see Table 2-4). Through the Centers for Medicare & Medicaid Services (CMS), the Federal Government administers the publicly financed health insurance programs of Medicaid and Medicare. Medicaid is the tax-based, jointly funded, federal-state assistance program that provides coverage of healthcare costs to low-income people who meet eligibility requirements. Eligibility for, and services covered under, Medicaid vary among states, and some cases require recipients to provide a copayment for services. Medicare is the federal health insurance program for persons 65 years or older, the disabled, and those with end-stage renal disease (ESRD). Medicare benefits are paid from an account that recipients have paid into during years of employment.

Prospective payment systems for healthcare services were instituted by the federal government in 1999 in an effort to control costs for these programs. In addition to the original Medicare fee-for-service program, Medicare offers beneficiaries the option to receive care through private insurance plans. These private insurance options are part of Medicare Part C, now called Medicare Advantage. The most common type of Medicare Advantage plans are health maintenance organizations (HMOs). Medicare Advantage is a means of receiving healthcare and Medicare coverage. The beneficiary must specifically opt to receive Medicare coverage and care through an HMO, or other private plan insurance. Once the choice is made, the beneficiary must generally receive all of his or her care through the plan’s providers in order to receive Medicare coverage. The main premise is that through preventive care and the use of a primary physician who acts as a gatekeeper to specialized care, healthcare costs can be reduced while beneficiary health can be maintained. Problems associated with Medicare Advantage plans are similar to those of patients receiving care from HMOs in that beneficiaries are limited to providers within the HMO, preapprovals are required for specialty care, and there is a complicated appeals process. Benefits to Medicare Advantage plans include reduced or absent deductibles and copays and no claim forms to complete.

With the passage of the Medicare Modernization Act of 2003 (MMA), Medicare Prescription Drug Coverage or Medicare Part D became available for Medicare beneficiaries, regardless of income, health status, or prescription drug usage. The Medicare Part D program provides beneficiaries with assistance paying for prescription drugs. Unlike coverage in Medicare Parts A and B, Part D coverage is not provided within the traditional Medicare program. Instead, beneficiaries must affirmatively enroll in one of many Part D plans offered by private companies. The Medicare law establishes a standard Part D drug benefit. Plans must offer a benefit package that is at least as valuable as the standard benefit. The standard benefit is defined in terms of the benefit structure, not the particular drugs that must be covered.

The standard benefit includes an initial deductible amount. After meeting the deductible, the beneficiary pays 25% of the cost of covered Part D prescription drugs, up to an initial monetary coverage limit. Once the initial coverage limit is reached, the beneficiary is subject to
another deductible, known as the Doughnut Hole or coverage gap, in which he or she must pay the full costs of drugs. When total out-of-pocket expenses on formulary drugs reach a second monetary coverage limit (including the costs of the deductible and coinsurance), the beneficiary reaches the Catastrophic Coverage benefit. A beneficiary entitled to Catastrophic Coverage pays a modest copay for a generic or preferred drug and a slightly larger copay for other drugs, or a flat 5% coinsurance, whichever is greater. This out-of-pocket amount is calculated annually. A beneficiary who reaches the out-of-pocket threshold in 1 year has to begin to meet it again on January 1 of the next year. Because the deductible, initial coverage limit, and annual out-of-pocket threshold change each year according to the changes in expenditures for Part D drugs, beneficiary out-of-pocket expenses may increase annually. The Medicare law does not mandate a set premium amount. These costs, as well as the list of covered drugs, vary from plan to plan and from region to region. Beneficiaries should take time to review the various plans available to them in light of their current and anticipated needs and financial resources.

Table 2-4. Health Insurance Programs

<table>
<thead>
<tr>
<th>Plan</th>
<th>Financing</th>
<th>Description</th>
<th>Covered Services</th>
</tr>
</thead>
<tbody>
<tr>
<td>Private health insurance</td>
<td>Private business and patient cost sharing</td>
<td>Indemnity: beneficiary reimbursed upon claim submission; service benefit: healthcare provider reimbursed upon claim submission</td>
<td>Physician services, hospital services, optional prescription benefit</td>
</tr>
<tr>
<td>Medicaid</td>
<td>Public (the Federal Government and state governments)</td>
<td>Assistance for healthcare; copays may be required</td>
<td>Physician services and limited prescription benefit</td>
</tr>
<tr>
<td>Medicare Part A</td>
<td>Public (Federal Government)</td>
<td>Hospital insurance (HI)</td>
<td>Care for patients in hospitals, skilled nursing facilities, hospice care, and home health services</td>
</tr>
<tr>
<td>Medicare Part B</td>
<td>Public (Federal Government)</td>
<td>Supplemental medical insurance (SMI)</td>
<td>Physician services, outpatient hospital care, durable medical equipment, preventive services, limited vaccines, and limited prescription benefit</td>
</tr>
<tr>
<td>Medicare Part C</td>
<td>Private insurance companies; patient premiums and copays</td>
<td>Medicare Advantage plans</td>
<td>Patients must have both Medicare Part A and Part B; provides Part A and Part B services and covers additional services</td>
</tr>
<tr>
<td>Medicare Part D</td>
<td>Public (Federal Government)</td>
<td>Prescription drug coverage, MTM</td>
<td>Outpatient prescription drugs, limited to formularies, and annual maximum; fee-for-service, PPOs</td>
</tr>
<tr>
<td>Medicare supplement</td>
<td>Private</td>
<td>MediGap</td>
<td>Portion of healthcare services for which the Medicare beneficiary has financial responsibility</td>
</tr>
<tr>
<td>Veterans’ benefits</td>
<td>Federal</td>
<td>Managed care provided within a closed system of veterans hospitals, clinics, and pharmacies</td>
<td>Hospitalization, home health, outpatient visits, prescription medications, and skilled nursing according to veteran’s eligibility</td>
</tr>
</tbody>
</table>
The MMA defines the drugs that are covered under Part D and, therefore, the drugs for which payment will be made under Part D in relationship to their coverage under Medicaid and under other parts of Medicare. A Part D drug is a drug that is approved by the FDA, for which a prescription is required and for which payment is required under Medicaid. Biological products, including insulin and insulin supplies, and smoking cessation drugs are also covered under Part D. The MMA excludes from coverage those categories of drugs for which Medicaid payment is optional. Of particular significance to Medicare beneficiaries is the exclusion of drugs for weight gain (used in connection with treating weight loss), barbiturates (used to treat seizures in older people), benzodiazepines, and over-the-counter (OTC) medications. Many of these excluded medications are used by geriatric patients. Part D plans are not required to pay for all covered Part D drugs. They may establish their own formularies or list of covered drugs for which they will make payment, as long as the formulary and benefit structure are not found by CMS to discourage enrollment by certain Medicare beneficiaries. Each drug plan must develop its own exceptions process, under which a plan enrollee may ask the drug plan to cover a nonformulary drug or to reduce cost sharing for a formulary drug. Prescription drug coverage under Part D is voluntary. A beneficiary may purchase Part D coverage if he or she is entitled to Part A or enrolled under Part B. The beneficiary does not have to have both Part A and Part B coverage to choose prescription drug coverage. The beneficiary must enroll in a Part D plan that serves the geographic region in which he or she resides. The Part D benefit is premised on the notion that individual Medicare beneficiaries should have a choice of private drug plans in order to select a drug benefit that best meets their needs.

An additional service available to those enrolled in Medicare drug plans is the Medication Therapy Management (MTM) program. MTM is a comprehensive medication review program provided by a pharmacist or other healthcare professional that includes a thorough review of medications, a personal action plan (relative to medications), and a comprehensive list of all medications taken by a patient. Medicare enrollees deemed eligible for MTM review include those with multiple chronic health conditions, multiple medications, and specific medication expenses.

Medicare Part D provides coverage for millions of American seniors who do not otherwise have prescription insurance, yet many seniors still lack prescription drug coverage. Its complex structure establishes barriers with selection of and enrollment in a prescription drug plan (formulary) that is the best fit for the individual geriatric patient. Also, there are limits on annual benefit amounts with associated out-of-pocket expenditures. Nursing home residents whose expenses are chiefly paid by Medicaid or private pay receive prescription drug coverage under Medicare Part D. Medicare Part D coverage in nursing homes is generally limited to plans that contract with long-term care pharmacies in order to ensure that the drug packaging and dosage forms needed are easily available. In addition, immunosuppressants, oral antineoplastics, oral antiemetics, inhalant solutions, and insulin, which are covered by Medicare Part B, are also covered under Medicare Part D, creating a dilemma with appropriate billing for the long-term care pharmacy.

The passage of the Affordable Care Act (ACA) in 2010 offered the promise of comprehensive health insurance reforms to include increased access to healthcare, improved quality of healthcare, lower healthcare costs, and new consumer protections. One of the features of ACA is the eventual phase-out of the Doughnut Hole or coverage gap in the Medicare Part D plan, expected to occur in 2020. CMS is currently reporting cost savings on Medicare Part D prescription drugs as a result of the implementation of ACA. The implementation of ACA in 2013 was both complex and controversial, and frequent changes have been made to the original legislation. The opportunities for pharmacist involvement in collaborative practice through
Accountable Care Organizations (ACOs), a key feature of the ACA, remain.\(^{46}\)

**Other Health Insurance Options**

Two common options available to seniors when selecting private health insurance are fee-for-service insurance and managed care plans: HMOs or preferred provider organizations (PPOs). Eligibility for private health insurance usually requires a medical examination to prove the patient is insurable, and the insured patient pays out-of-pocket premiums and deductibles for healthcare services. Some employers provide health insurance, which includes prescription drug coverage for vested retirees. The Department of Veterans Affairs (VA) provides healthcare to veterans, dependents, and survivors according to eligibility; nearly 45% of veterans in the United States are over the age of 65 years, and 9.73 million veterans are enrolled in the VA healthcare system.\(^{47}\) A joint Medicaid and Medicare program known as PACE (Programs of All-inclusive Care of the Elderly), is available in many states to allow seniors who need more care to remain in the community and receive healthcare services at home, if they reside in the service area of a PACE organization and meet the eligibility criteria.

**Challenges of Existing Models of Healthcare Financing**

The geriatric population, those 65 years of age and older, accounts for 36% of all hospital stays, 49% of all days of care in hospitals, and consumes almost one-third of the total U.S. healthcare expenditures.\(^{48}\) Although geriatrics compose about 12% of the U.S. population, they account for 34% of all prescription medication expenditures and 25% of OTC medication usage.\(^{49}\) An estimated 91% of the U.S. population aged 65 and older has an annual prescription drug expense. In 2013, there were over 35 million Medicare Part D enrollees, an increase of 12% from 2012.\(^{50}\)

The existing models of U.S. healthcare financing ultimately limit the individual patient's autonomy in making choices related to healthcare. The challenge is in achieving a balance between the access to healthcare and the provision of effective and affordable healthcare. Private health insurance plans commonly have prescription drug benefits, but these may be rigid in requiring the patient to purchase maintenance prescriptions from specific pharmacies or from mail-order pharmacies, use formularies with associated tiered copayments for the prescribing of brand name drugs over generic drugs, and/or require prior authorization from the third-party payer for use of certain brand name drugs or drug classes.

When choosing between independent community pharmacies and chain community pharmacies for pharmacy services, ambulatory geriatric patients often price shop for prescriptions in a competitive market made more widespread by the recently implemented inexpensive generic offerings at chain pharmacies. When seniors are admitted to long-term care settings, either an assisted living facility or a skilled nursing facility, their choice of a provider of pharmacy services may be limited to those that can provide the medications in the packaging system used by the facility and/or those pharmacy providers who can provide the federally mandated consultant pharmacy services to the residents of the facility. Pharmacy services for residents of long-term care settings are further complicated by the increasing use of formularies to manage prescriptions and control costs. Complications arise from the need to educate prescribers on the use of formularies and state pharmacy regulations regarding medication substitution issues.

The emergence of managed care as a major healthcare force affecting older persons raises its own set of ethical issues. Whereas managed care offers older persons some attractive advantages, its propensity to reduce access to choice of care can be a major threat to healthcare for the more frail older patients. Geriatric patients are prime targets for efforts aimed at rationing healthcare because they consume disproportionately large amounts of medical care and because they are seen as having already lived
their lives. Within the efforts to limit spending on older people, subtle approaches have been used and are cloaked in ethical concepts. Policy issues largely address questions of access and coverage, but these can be influenced by an individual clinician’s beliefs about what elements of care are appropriate for older people. These beliefs, in turn, can reflect stereotypes and, therefore, ethical issues arise at the bedside when decisions about initiating or continuing treatment are made.\(^\text{38}\)

The geriatric patient is often in a state of dependency, and there is disagreement on the value of a life lived with some level of dependency. If the level of dependency is the primary outcome of healthcare, this implies that those who are dependent are no longer important to society. Much attention has been given to the money spent on healthcare in the last year of life. Costs related to healthcare increase when death approaches; the costs during the last month of life represent approximately 40% of the total costs for the last year of life.\(^\text{51}\) Approximately 28% of the Medicare budget goes to the 5% of Medicare patients who die each year.\(^\text{52}\)

In the provision of pharmaceutical care for geriatric patients, pharmacists have an obligation to work with patients, their caregivers, and third-party payers to ensure that older patients receive the most appropriate medications to manage their health problems. Pharmacists should be prepared to discuss both the benefits and the limitations involved in obtaining affordable prescription medications, including the use of OTC medications in lieu of prescription medications, generic drugs, pill-splitting, tiered copayment benefit plans, prescription drug plans, mail-order pharmacies, Internet pharmacies, and prescription assistance programs from State Pharmacy Assistance Programs (SPAPs) community coalitions, nonprofit organizations, and the Pharmaceutical Research and Manufacturers of America (PhRMA).
Case 1: Skilled Nursing Facility

Subjective:
SS is a 90-year-old female who has been a resident of a skilled nursing facility for 8 years.

Past Medical History:
Late-stage Alzheimer disease; heart failure; receives nutrition via a nasogastric tube; confined to bed; occasional urinary incontinence. Within the past year, SS has been hospitalized four times due to the heart failure.

Medications:
Donepezil 10 mg at bedtime, aspirin 81 mg once daily, lisinopril 10 mg once daily, HCTZ 12.5 mg once daily, acetaminophen 650 mg every 6 hours as needed for pain (all medications are administered via the nasogastric tube).

Allergies:
NKDA.

Social History:
BK (SS’s daughter) is a court-appointed guardian for SS and has had the physician sign a DNR order.

Family History:
Noncontributory.

Objective:
BP 126/76, P 76 BPM, RR 24, oral T 97°F, Ht 5’1˝, Wt 118 lb.

Physical Examination:
Chest examination revealed dyspnea, productive cough, rhonchi.

Labs:
Sputum gram stain reported as: >25 WBC/hpf, <10 epithelial cells/hpf, many Gm (+) cocci in pairs. C&S reported as Mycoplasma pneumonia. Sensitive to erythromycin and azithromycin.

Assessment:
SS is a 90-year-old female with community-acquired pneumonia, cardiac risk factors, poor nutritional status, occasional urinary incontinence, and poor cognitive status. Signed DNR order is in the medical record.

Intervention:
Forty-eight hours after the above assessment was written, RT, the consultant pharmacist for the facility, is completing the monthly drug regimen reviews. During the chart review for SS, RT noted the patient’s diagnosis of community-acquired pneumonia with no order for antibiotic therapy. When RT questioned the nurse regarding the lack of an order for an antibiotic, the nurse responded that because the patient is DNR, “No antimicrobial therapy is warranted in this situation.”

Plan:
Contact physician for antibiotic order, as patient is not in cardiac or respiratory arrest.
Fundamentals of Geriatric Pharmacotherapy

Rationale:

1. The court-appointed guardian for SS has had the physician sign a DNR order. At this point, the patient is not in cardiac or respiratory arrest, so an antibiotic should be ordered.

2. The physician has a professional responsibility to SS to order an antibiotic to treat the pneumonia. The pharmacist has a professional responsibility to contact the physician and obtain an order for an antibiotic to treat the pneumonia.

3. The ethical issues raised in this scenario include respect for patient autonomy (right to self-determination) and surrogate decision making, beneficence (help others and promote patient welfare), and nonmaleficence (at least do no harm). If the pharmacist did not follow up with the physician to obtain an order for an antibiotic, the pharmacist would not respect the surrogate decision and would place SS in harm. Compare this ethical dilemma to the following scenario.

SCENARIO TWO

Subjective:
SS is a 90-year-old female who has been a resident of a skilled nursing facility for 8 years.

Past Medical History:
Late-stage Alzheimer disease; heart failure; receives nutrition via a nasogastric tube; confined to bed; occasional urinary incontinence. Within the past year, SS has been hospitalized four times due to the heart failure. Within the past 3 months, SS has developed recurrent pneumonias with subsequent deterioration after each one (a total of four) pneumonias, each requiring hospitalization in addition to the four episodes with heart failure exacerbation.

Medications:
Donepezil 10 mg at bedtime, aspirin 81 mg once daily, lisinopril 10 mg once daily, HCTZ 12.5 mg once daily, acetaminophen 650 mg every 6 hours as needed for pain (all medications are administered via the nasogastric tube).

Allergies:
NKDA.

Social History:
BK (SS’s daughter) is a court-appointed guardian for SS and has had the physician sign a DNR order.

Family History:
Noncontributory.

Objective:
BP 126/76, P 76 BPM, RR 24, oral T 97°F, Ht 5´1˝, Wt 118 lb.

Physical Examination:
Chest examination revealed dyspnea, productive cough, rhonchi.

Labs:
Sputum gram stain reported as: >25 WBC/hpf, <10 epithelial cells/hpf, many Gm (+) cocci in pairs. C&S reported as Mycoplasma pneumonia. Sensitive to erythromycin and azithromycin.
**Assessment:**
SS is a 90-year-old female with community-acquired pneumonia (fourth pneumonia in 120 days with subsequent deterioration following each case), cardiac risk factors, poor nutritional status, occasional urinary incontinence, and poor cognitive status. Signed DNR order is in the medical record.

**Intervention:**
Forty-eight hours after the above assessment was written, RT, the consultant pharmacist for the facility, is completing the monthly drug regimen reviews. During the chart review for SS, RT noted the patient’s diagnosis of community-acquired pneumonia with no order for antibiotic therapy. When RT questioned the nurse regarding the lack of an order for an antibiotic, the nurse responded that the physician stated, “No antimicrobial therapy is warranted in this situation.” She further describes a consultation between the physician and the court-appointed guardian for SS (the daughter) where the daughter stated that she understood her mother will not return to her previous level of functioning. The daughter stated that her mother would not wish to continue with multiple infections and poor quality of life. The surrogate decision is made to place SS in hospice.

**Plan:**
Withhold antibiotics. Ensure pain and other symptom management is optimized.

**Rationale:**
Respect patient autonomy and withhold antibiotics. Ensure beneficence by ensuring patient is kept comfortable.
Case 2: Community Pharmacy

Subjective:
WW is a 78-year-old male retired from the telecommunications industry. He lives in his private residence with his wife of 56 years. He has no current health-related complaints.

Past Medical History:
Type 2 diabetes, hypertension, hyperlipidemia, depression, osteoarthritis, and macular degeneration.

Medications:
Pioglitazone 15 mg every morning, metformin 1000 mg twice daily, losartan 25 mg twice daily, furosemide 40 mg once daily, ezetimibe/simvastatin 10/40 once daily at bedtime, celecoxib 100 mg twice a daily, venlafaxine XR 75 mg every morning, aspirin 81 mg once daily, Ocuvite once daily.

OTC Medications:
Multivitamin (senior formula) once daily, meclizine 25 mg as needed, calcium carbonate 500 mg as needed, docusate sodium 100 mg twice daily, fish oil 1000 mg twice daily, biotin 1000 mcg once daily, garlic 1000 mg once daily, purchases diabetic supplies to check blood glucose four times a day with a glucometer.

Allergies:
Penicillin, radioactive dyes.

Social History:
Negative for tobacco and alcohol; receives Medicare Part D benefits.

Family History:
Unknown.

Objective:
BP 166/78 (on self-check BP machine in the pharmacy), Ht 6’2”, Wt 196 lb.

Physical Examination:
WDWNWM in no acute distress.

Labs:
Not available; WW stated that at his last physical (2 months ago) “Everything was A-OK!”

Assessment:
WW is 78-year-old male with elevated blood pressure who presents at the pharmacy counter and asks to speak with the pharmacist about the cost of his medications.

Plan:
1. Review WW’s patient profile and complete a medication therapy management plan for WW.
2. Discuss with WW available alternatives for obtaining affordable prescription medications and reducing medication costs.
Rationale:

1. The older patient is frequently on a complicated medication regimen that often includes OTC products and dietary supplements. Pharmacists should develop MTM plans especially for geriatric patients. Pharmacists should discuss these medication therapy plans with patients to ensure they understand the indication and directions for use of each medication in their regimen.

2. Pharmacists should work with elderly patients to ensure that those enrolled in Medicare Part D prescription drug plans are enrolled in one with a formulary most appropriate for their medication profile; generic alternatives are being dispensed when available; the most appropriate tiered copayment drugs are prescribed; patients are receiving medications from mail-order pharmacies, if appropriate; patients are informed of the advantages and cautions of ordering prescription medications from Internet sources; prescription assistance plans available from community coalitions, nonprofit organizations, and PhRMA are maximized for the patient’s benefit.
**Clinical Pearls**

- A geriatric patient who refuses aggressive (and expensive) chemotherapy for treatment of advanced stage breast cancer with the desire to preserve her children’s inheritance is exerting personal autonomy in decision making. A clinician must defer to the patient’s wishes to honor the ethical principle of autonomy even if he or she disagrees with the patient’s decision.

- When considering the risk-to-benefit ratio of a medication with potentially severe adverse effects (e.g., aspirin for myocardial infarction prophylaxis in a frail elderly patient), the pharmacist should take into consideration the patient’s remaining life expectancy, the time required to obtain benefit from the medication, the goals of care, and the treatment targets.

**Chapter Summary**

The tenets of biomedical ethics are important to the provision of healthcare and pharmaceutical care for the geriatric patient. Pharmacists respect patient autonomy by allowing patients to exercise their right of self-determination; display nonmaleficence when they act to prevent harm for the patient; display beneficence when they act for the good of the patient; and demonstrate justice when they allocate goods and services to their patients in an equitable manner.

Communication and decision making are important in providing healthcare for geriatric patients. Health care practitioners in general, and pharmacists specifically, should strive for effective communication with geriatric patients and assist them in having their personal choices regarding healthcare decisions made known and accomplished. Although a major benefit of managed care is that of shared risk, in reality the current healthcare system has the potential to limit access to healthcare choices for geriatric patients.

Through the provision of accessible, convenient, confidential, and appropriate pharmaceutical care, the pharmacist can contribute to the resolution of healthcare disparities in the geriatric patient population. It is the professional responsibility of pharmacists to serve as patient advocates to ensure that these patients receive the pharmaceutical care to which they are entitled and that they desire.

**Self-Assessment Questions**

1. What is the difference between a living will and a durable power of attorney for healthcare?

2. How do informed consent, privacy, and confidentiality affect decision making in geriatric patient care settings?

3. What constitutes life-sustaining therapy?

4. What is the difference between palliative care and hospice care?

5. How do socioeconomic issues contribute to healthcare disparities within geriatric patients, specifically in relation to medication adherence?

6. What are the differences between Medicaid and Medicare in terms of financing, eligibility, and benefits?

7. What options are available for geriatric patients to obtain affordable prescription medications?
1. Pozgar GD. Legal and Ethical Issues for Health Professionals. Sudbury, MA: Jones and Bartlett; 2005.


Learning Objectives

1. Compare the theories of biological aging.
2. Define successful aging.
3. Summarize the common physiologic changes associated with aging.
4. Outline the pharmacokinetic alterations that affect drug dosing in the elderly patient.
5. Identify age-related changes in pharmacodynamic sensitivity to medications.
6. Alter a standard drug regimen based on pharmacokinetic and pharmacodynamic changes expected in an older adult.

Key Terms and Definitions

FRAILTY: Loss of reserve in interrelated physiological systems that prevents a normal response to stressors, delaying or preventing the return to homeostasis.

FUNCTIONAL DECLINE: Limitations developed over time in physical, cognitive, and social activities that prevent an older adult from performing activities of daily living or maintaining his or her desired quality of life.

GROWTH HORMONE: The peptide hormone, also called somatotrophin, which stimulates human cell growth and reproduction. The generic name of the recombinant deoxyribonucleic acid (DNA) human growth hormone marketed in the United States is somatropin.

OXIDATIVE STRESS: Damage to a living cell as a result of normal oxidation reactions in the mitochondria that produce free oxygen radicals or free radical species generated by nonmitochondrial sources (e.g., the cytochrome P450 enzymes in the microsomes, phagocytic cells during inflammation reactions).

SUCCESSFUL AGING: No single definition of successful aging has been accepted, but most believe it requires the achievement of old age with few or no diseases or disabilities, high physical and cognitive functioning, and active engagement with life.
**Introduction**

The pharmaceutical care of older adults differs from that of younger adults for multiple reasons. Furthermore, considerations for the frail elderly are different from those of the healthy elderly patient. This chapter will focus on the biologic changes that influence the use of medications in the elderly. After reviewing the most widely accepted theories of aging, the chapter will start with an overview of the physiologic changes commonly seen with aging to provide the background for understanding changes expected in medication use. When these factors are considered prior to treatment, drug-related problems can be minimized. Although individually these factors appear straightforward, it is the need to integrate biologic changes seen in aging to design an optimal therapeutic regimen that increases the complexity of care in this population. Such are the challenges for the healthcare provider working with geriatric patients.

**Physiology of Growing Older**

There are commonly recognized physical characteristics associated with aging (e.g., hair graying, baldness, wrinkles), but no specific biomarkers predict morbidity or mortality due to aging. Because of this, one cannot make far-reaching assumptions regarding the magnitude of age-related biological changes for each individual at the last stages of adulthood. However, age remains the most significant risk factor for predicting death, so researchers continue to explore theories of aging in an effort to identify interventions that would reduce the significance of this risk factor.¹

**Theories of Aging**

The multitude of differences seen in the aging adult contributes to a multitude of theories that attempt to explain the biology of aging. In the 1990s, over 300 theories had been proposed.² Currently these theories are classified into two major categories: damage theory and programmed biology theory.³

**Damage Theories**

*Damage theories* of aging focus on environmental stressors to the cells and include the *oxidative stress* theory, wear-and-tear theory, and the telomere theory. The *oxidative stress theory* proposes that aging occurs as a result of damage from free oxygen radical species normally produced within the cell, particularly by the mitochondria and the cytochrome P450 (CYP450) systems.²,⁴ Once the cell's antioxidant defenses are unable to protect the cell from these free radical species, the oxidative damage accumulates and causes aging. This theory has support from many investigators who have used flies, worms, and rodents to show the impact of lower and higher oxidative stress.⁵ The oxidative stress theory is also supported by epidemiologic studies in humans, which indicate that people who consume a diet high in antioxidants found in fruits and vegetables live longer, healthier lives.⁴,⁶ However, randomized, prospective studies that used vitamin E, A, and C supplements in an attempt to reduce the morbidity or mortality of age-related diseases (cardiovascular, dementia) have not shown effectiveness.⁷,⁸

The *wear-and-tear theory* is related to the oxidative stress theory but is not grounded on the generation of free oxygen radicals within the cell. Instead, it proposes that aging is the effect of the physiological work of cells, and this work is indirectly related to the organism's adverse living conditions.² Therefore, stressful living conditions would increase the work of cells and reduce lifespan. Other related theories, such as the error catastrophe or somatic mutation theories, focus on random molecular damage to DNA that accumulates over time, until the genetic material can no longer be expressed or proteins produced are changed and ineffective.

Another cellular theory of aging, the *telomere theory*, centers on the tendency for normal human cells to have a finite number of replications before the cell's telomeres shorten and are no longer able to support cell division. The telomeres provide handles for moving chromo-
somes, and once they become too short, they are no longer functional and the cell cannot divide. This finite number is termed Hayflick’s limit, after the scientist who first described it. Cancerous cells do not experience the shortening of the telomeres and can divide an infinite number of times.9

Programmed Theories
Programmed theories of aging are based on the idea that aging follows a biologic clock. One subset of this category focuses on genetic regulation of cell function, which suggests aging occurs due to changes in gene expression that regulate the organism throughout all phases of life. Just as genes direct the body of an infant to grow and develop, they also direct the body of an octogenarian to decline and fail. Gene expression within a cell is thought to initiate cell death; this is termed apoptosis.9

The immune system closely interacts with the neuroendocrine system to control and eliminate foreign organisms from the body without destroying the host. Failure of the immune system weakens the body’s ability to fight infections or to police for cancerous cells. This failure to recognize “self” triggers the failure of the body to survive. Mature T cells from healthy older adults as compared to frail elderly patients do not show a decline in function or adaptability, providing support for this theory.9

Another programmed theory identifies that changes in the ability of the hypothalamic-pituitary-adrenal (HPA) axis occur and signal each stage of life. In the final stage, the neuroendocrine system is unable to adapt to new stressors from the environment, leading to decline and death.10 Many individuals believe that every organism has its own biological clock, which is programmed for the life expectancy of the species and the specific organism fitting into this line of thinking.

KEY POINT: No single theory of aging is able to explain all of the changes that occur and lead to senescence of the individual.

Age-Related Biological Changes

Cardiovascular
A large body of literature is devoted to cardiovascular changes seen with aging. But because cardiac disease is the leading cause of death in elderly patients, it is important in these studies to separate the changes seen with normal aging compared to those seen commonly with aging due to cardiovascular diseases. Morphologic changes that are thought to be due to aging alone include a decrease in myocytes within the myocardium, hypertrophy of the remaining myocytes, a stiffening of the ventricles, a reduced number of pacemaker cells in the sinoatrial node, valvular dilation and calcifications, and stiffening of the arterial wall.11 These morphologic changes lead to a reduced ability to relax the heart (diastolic dysfunction) and a loss of the early filling from the atrial contraction. These changes can be seen on an echocardiogram, which shows an elevated left ventricular end-diastolic pressure and a reversal in the ratio of early to late filling velocity (E/A ratio).

The stiffening of the aorta and other large arteries predisposes the elderly patient to isolated systolic hypertension because the large vessels can no longer absorb the high pressures from systolic contraction of the heart. In turn, this predisposes the patient to orthostatic hypotension and syncope, as the body is unable to compensate for the drop in pressure due to a diminished baroreceptor reflex tachycardia and peripheral vasoconstriction.11

Persistent elevation of catecholamines leads to a desensitization of beta-adrenergic receptors. The maximum predicted heart rate with exercise decreases with aging and has not shown to be reversible with athletic training. Endothelial dysfunction is also seen with aging, possibly due to diseases such as hypertension, diabetes mellitus, and dyslipidemias.11

Central Nervous System
Many older adults complain of memory loss, especially the very old, even when neuropsychological test results do not show cognitive impair-
Normal changes seen with aging include decreases in brain mass, cerebral blood flow, and cerebral autoregulation. Dopaminergic, muscarinic, and serotonin receptors tend to decrease, although this decrease has not been directly associated with abnormal thinking. Crystallized cognitive abilities (i.e., vocabulary, accumulated knowledge, understanding proverbs) increase over the lifespan and remain intact throughout the normal aging process. However, fluid abilities (i.e., mental speed, novel problem solving), which rely more on short-term memory storage, peak in the mid-twenties and slowly taper until the mid-sixties. At this point, a steeper decline occurs. Fluid abilities are more affected by injury and disease, so their decline may not be solely due to normal aging, and most elderly people readily compensate with this decline through crystallized intelligence.

The efficiency of sleep (the amount of time spent in bed asleep) decreases with aging. Older persons tend to take the same amount of time to fall asleep as younger adults, but they spend more time in Stage 1 and 2 non-REM (rapid eye movement) sleep and less time in Stage 3 and 4 REM sleep. More awakenings contribute to the reduction in sleep efficiency, and elderly persons frequently complain of nonrestorative sleep problems. This leads to daytime napping and an earlier bedtime.

Renal and Genitourinary

Kidney mass and weight decline by 10% to 43% over the lifespan. The number of glomeruli decreases, and the glomerular basement membrane thickens. Hence, glomerular function declines significantly with aging, and the kidney has an increasingly difficult time maintaining fluid and electrolyte balance when presented with restrictions or overloads. The serum creatinine, a traditional indicator of renal function, may not increase in proportion to the decrease in kidney function due to the decrease in muscle mass seen in older adults. Tubular function is also impaired, such that the kidney will not reabsorb sodium in concert with the body’s needs. When dietary sodium restrictions are imposed, the kidney does not respond rapidly and sodium losses continue in the tubules for a time. It is unwise to strictly limit sodium intake for most elderly patients.

The kidney’s ability to dilute or concentrate the urine is also impaired with aging, most likely due to a loss of concentrating ability of the medullary tissue. Elderly patients have difficulty maintaining appropriate volume status if volume depletion or overload occurs.

The urinary tract is also changed with aging. For women, the loss of estrogen with menopause may cause atrophic urethritis and diminished urethral resistance, and the process of child-bearing may cause weakening of the pelvic floor muscles. Although urinary incontinence is not considered a part of normal aging, these changes increase the risk for urinary incontinence due to stress or urge. Men may develop an enlarged prostate leading to urinary obstruction and an increased risk for overflow incontinence.

Endocrine

Changes in the endocrine system have been associated with aging and aging theories. While some important hormones decrease with age, many others maintain secretion patterns and quantities that match those of young and middle-aged adults; still others are increased in the body’s effort to maintain homeostasis (see Table 3-1). Several hormones secreted through the HPA axis do not deteriorate with aging. Concentrations of adrenocorticotropic, cortisol, and antidiuretic hormone remain unchanged throughout the lifespan. Although levels of epinephrine and norepinephrine are higher in older adults than in younger adults, the response to stress is not blunted, with hormones secreted through the HPA axis or the catecholamines. The thyroid decreases in size, and fibrosis and lymphocytic infiltration increases within the gland. In spite of this, the serum concentrations of thyroxine and thyroid stimulating hormone (TSH) do not change significantly with aging unless disease is present. Insulin concentrations tend to increase with age, although this may be due to the increase in percentage of body fat, which causes an increase in insulin resistance.
**Table 3-1. Hormone Changes Seen with Aging**

<table>
<thead>
<tr>
<th>Decreased Concentrations</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Estradiol</td>
<td>Rapid increases and decreases seen during perimenopause, with gradual reductions</td>
</tr>
<tr>
<td>Testosterone</td>
<td>Slow, subtle decrease after age 50</td>
</tr>
<tr>
<td>DHEA</td>
<td>Gradual decrease</td>
</tr>
<tr>
<td>Growth hormone</td>
<td>Pulse amplitude and duration decrease. Pulse frequency is maintained</td>
</tr>
<tr>
<td>Calcitonin</td>
<td>Total decreased, but active levels intact</td>
</tr>
<tr>
<td>Renin</td>
<td>Significant decreases from sixth decade onward</td>
</tr>
<tr>
<td>Aldosterone</td>
<td>More difficult to maintain sodium and potassium balance</td>
</tr>
<tr>
<td>Erythropoietin</td>
<td>Relative to decrease in kidney size and function</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>No Change in Concentration</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>ACTH</td>
<td>No change, but earlier daily peak</td>
</tr>
<tr>
<td>Cortisol</td>
<td>Response to stress maintained</td>
</tr>
<tr>
<td>Antidiuretic hormone</td>
<td>Impairs ability to maintain fluid balance</td>
</tr>
<tr>
<td>Glucagon</td>
<td></td>
</tr>
<tr>
<td>Prolactin</td>
<td>Nocturnal pulsatile secretion lost</td>
</tr>
<tr>
<td>Thyroxine</td>
<td>T4 levels preserved, T3 levels reduced</td>
</tr>
<tr>
<td>Thyrotropin-stimulating hormone</td>
<td>No change or may rise with age</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Elevated Concentrations</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Epinephrine</td>
<td>Response to stress maintained</td>
</tr>
<tr>
<td>Norepinephrine</td>
<td>Response to stress maintained</td>
</tr>
<tr>
<td>Atrial natriuretic peptide</td>
<td>Increased due to renal resistance; leads to impaired salt wasting and difficulty in handling a decrease in salt intake, leading to volume depletion with low-sodium diet</td>
</tr>
<tr>
<td>Insulin</td>
<td>Increased due to increased peripheral tissue resistance</td>
</tr>
<tr>
<td>Parathyroid hormone</td>
<td>Increased to maintain serum calcium levels</td>
</tr>
</tbody>
</table>

Hormones that significantly decrease with normal aging include estrogen in women, testosterone in men, growth hormone, and dehydroepiandrosterone (DHEA). Menopause occurs when cyclic estrogen production from the ovaries is replaced by a low continuous production at about 20% of pre-menopausal levels. This leads to uterine atrophy and a decrease in vaginal secretions, which may further lead to dyspareunia and a decline in libido. In addition, hot flashes accompanied by perspiration, tachycardia, and vasodilation of the skin are reported in 50% to 75% of peri-menopausal women, frequently interrupting sleep. The mean age for menopause is 50 years, so most elderly women have had ample time to adjust to post-menopausal changes. However, if a patient has been treated with estrogen therapy through these years and subsequently has therapy discontinued, she is at risk for experiencing peri-menopausal symptoms.
The aging male does not experience the abrupt discontinuation of sex hormone production found in women. Testosterone production declines slowly over time, with many men never reaching a level where they would be considered androgen deficient. Sexual responses become slowed, decrease in intensity, and exhibit an increase in refractory period. And, although the number of spermatozoa decreases, reproduction can take place even at the extremes of age for men.\textsuperscript{15}

Growth hormone secretion by the pituitary diminishes with age regardless of continued secretion of growth hormone releasing factor in the hypothalamus. This hormone is responsible for maintenance of muscle mass and strength. DHEA concentrations in 85-year-old individuals are one-fifth that of 30-year-olds. Although the exact action of DHEA in humans is not clearly understood, animal studies indicate that it plays a role in prevention of obesity, diabetes mellitus, cancer, and heart disease.\textsuperscript{16}

**Gastrointestinal**

Gastrointestinal complaints are frequently expressed by older patients; however, many of these complaints are due to pathologic processes rather than a result of aging. For example, no important changes occur in the oral cavity that are strictly due to aging. Rather, poor oral hygiene and lack of fluoridated water sources in childhood contribute to poor dental health in older adults. Dry mouth is most often due to anticholinergic medications instead of aging. Esophageal function is preserved with aging except in patients with neurologic diseases, such as neuropathy or stroke.\textsuperscript{18}

The stomach, small intestine, and large intestine are primarily unchanged with aging. Some researchers have noted atrophy of the stomach and of the villi in the small intestine that was believed to be associated with aging, although others have found no changes when disease was ruled out as a cause. Atrophic gastritis with a resultant achlorhydria, once thought to be universal with aging, is now known to be associated with pernicious anemia or infection by Helicobacter pylori.\textsuperscript{16} Peristalsis may be slowed with aging, resulting in an increased satiety from filling in the stomach and constipation from slowed emptying through the large intestine. Yet this commonly shared belief is not substantiated for all elderly persons.

The size and blood flow to the liver decrease as much as 1.5% per year after age 50. The number of hepatocytes is decreased, and protein synthesis is diminished. The pancreas size may or may not be reduced with aging. Even with these changes, the normal function of the liver and pancreas is not appreciably altered, as there is a tremendous reserve capacity in these two organs.\textsuperscript{19}

**Musculoskeletal and Connective Tissue**

Muscles, skin, and bones undergo many changes within the aging adult. Lean muscle mass changes dramatically, with an average decrease of 30% to 40%. This change may be due more to an increasingly sedentary lifestyle than strictly to aging itself. Nonetheless, elderly patients tend to replace lean body tissue with fat tissue over time unless they continue a rigorous exercise routine.

Skin changes are either intrinsic or extrinsic. Intrinsic changes include thinning of the skin and loss of elasticity. Extrinsic changes are related to the amount of time the skin has been exposed to the sun and are synonymous with photoaging. Sun exposure leads to fine and coarse wrinkling of the skin, leathery texture, telangiectasias, actinic keratoses, and a blotchy appearance. Generally, one can compare skin changes from the face or hands with the skin from the patient’s buttocks to identify the differences between intrinsic and extrinsic aging. Body hair also may gray, thin, and finally be lost altogether with aging except for hair on the face. Sebum secretion decreases with age, leading to dry, coarse skin and xerosis. Sweat glands also diminish with age, and thermoregulation becomes more difficult as one grows older. These changes decrease the skin’s ability to prevent infection.\textsuperscript{20}

Bone remodeling occurs throughout the lifespan, but after age 30, there is a net bone loss of 0.7% to 1% per year. Bone loss is accelerated
after menopause in women for approximately 5–10 years, after which it stabilizes.21 The relative increase in bone resorption increases the risk of fracture in the elderly patient. Older individuals lose height at a rate of 0.6 cm per decade, mostly due to loss of height of the vertebrae and narrowing of the vertebral discs. This decrease is accelerated when compression fractures of the vertebra occur, leading to kyphosis. The long bones of the arms and legs do not shorten over time.

**Respiratory**

The lung tissue loses elasticity with age, but this is counterbalanced by changes in the chest wall and muscles so that total lung capacity is not changed. However, older individuals are unable to move air in and out of the lungs as quickly as younger individuals, and all measures of air flow (e.g., forced expiratory volume in the first second [FEV1], forced vital capacity [FVC]) decrease with age. In addition, there is an increase in residual lung volume and dead air space, partly related to more rapid closure of small alveoli on expiration. This rapid closure, termed closing capacity, contributes to a reduction in arterial oxygen tension, which falls linearly in association with age.22

**Immunology/Hematology**

Hemoglobin levels decrease with age, but this is more likely a phenomenon secondary to decreased erythropoietin synthesis due to decreased kidney size and function. In very old men, loss of testosterone may influence hemoglobin production. Other contributing factors could be the presence of chronic inflammation, a vitamin B12 deficiency, or iron loss, none of which are due to aging. Therefore, anemia is not normal with aging but is frequently encountered.16

Immunocompetence declines with age. This corresponds to one of the programmed theories of aging. The thymus decreases in size after puberty, which affects T cells and cell-mediated immunity. Humoral immunity appears to be decreased as well, with a lessened production of antibodies in response to antigen stimulation. In general, the older, frail patient is unable to mount the same immune response to an infectious insult, so we do not always see swelling, pain, or erythema at the site of an infection. Moreover, many elderly patients do not mount a fever or leukocytosis in response to systemic infections. This altered presentation makes diagnosis and monitoring of therapy difficult in the elderly patient.10

**Sensory**

Visual changes are universal with aging. By the age of 55, corrective lenses for reading and/or distance vision are needed by almost everyone. The loss of near vision associated with aging is called presbyopia. Accommodation to changes in lighting is more sluggish, and glare becomes a problem. The ability to distinguish colors, particularly between greens and blues, is lost. Cataracts are likely to develop by the age of 70. Functional blindness increases with age to a prevalence of 17% in those age 90 and older.21

Hearing changes result from multifactorial changes seen with aging. First, cerumen in the ear canal is dryer and more likely to become impacted, which can contribute to hearing loss. Secondly, the inner ear may suffer degenerative changes, particularly from exposure to noise or atherosclerosis. This leads to loss of high frequency hearing, referred to as presbycusis. Medications can contribute to hearing loss. Specifically, aminoglycosides, vancomycin, and loop diuretics have been shown to cause irreversible hearing loss.21,23

Taste and smell perceptions also show decline in older adults. By the age of 80, the ability to perceive smells is reduced in half. Taste is less predictable, but some studies show that a higher threshold is required for sour, bitter, and salty tastes but not for sweet tastes. Before one assumes a change in taste is due to aging alone, medications such as metronidazole and captopril should be evaluated for their potential to cause dysgeusia. These changes are important to address for patients with reduced appetite and malnutrition.21
Geriatric Syndromes

Medical research and practice typically revolve around a linear model, in which a disease occurs through a known etiology, following a defined pathogenesis until classic, characteristic symptoms emerge. There is some variability in the presentation, but generally these variations are known. However, a geriatric syndrome does not follow this typical linear pathway. Instead, signs and symptoms of a geriatric syndrome result from multiple causes that have interacted with accumulated dysfunctions of multiple organ systems. A concentric model interacting with multiple risk factors is more descriptive. In other words, the decline in function of various organs within the older adult, coupled with other age-related risk factors, results in the development of a clinical condition called a geriatric syndrome.

Examples of geriatric syndromes include delirium, falls, polypharmacy, and constipation. Treatment is directed toward the symptoms while simultaneously attempting to identify and correct the underlying causes. A young patient presenting with constipation is evaluated for a specific cause (frequently low dietary fiber), which is then treated with a medication to cure the cause (high-fiber diet and psyllium). However, in the older adult, constipation occurs due to multiple interacting factors. The gastrointestinal tract normally slows with aging and patients are less active (a risk factor for constipation); these issues synergistically interplay with the patient taking multiple medications that cause constipation. The clinician must treat the symptoms effectively and identify underlying multiple etiologies, making decisions as to what medications can be changed and which ones must be continued, frequently adding additional medications to the regimen that may further exacerbate the geriatric syndrome of polypharmacy. Geriatric syndromes make research and management of the older adult challenging.

Concepts of Successful Aging

With more individuals living into their eighties and nineties, a greater interest has developed among the lay public, clinicians, and researchers about what constitutes successful aging. It is universally agreed that living longer is not enough to be “successful” if functional abilities are severely compromised. Although the simplistic view that successful aging may be a product of an increased quantity of years plus an increased quality of years, more specific definitions and models to measure successful aging are needed.

The biomedical model focuses on longevity plus the absence of diagnosed chronic medical diseases, no psychiatric illness, and little or no difficulty with the activities of daily living. Some researchers include participation in social activities as a part of this model. The social functioning model focuses on the number of different social activities and the frequency of social contacts. Psychological models include measurement of self-efficacy, coping, self-worth, and goals. Socioeconomic models also exist. One of the strongest influences of self-perceived quality of life is an individual’s feeling of being in control of his or her life and the presence of a positive attitude toward problems. Different cultures endorse different components of successful aging as important. For example, independence is more important to European Americans, whereas Japanese older adults select social belonging as more important. Biomedical models tend to neglect cognitive and emotional aspects of successful aging as well as the role that adaptation to disability has in an individual’s perspective of successful aging.

KEY POINT: For pharmacotherapy decisions to be tailored to the patient’s needs and desires, the clinician must approach each patient individually to identify which areas constitute that person’s definition of successful aging.

Because the definitions of successful aging are still developing, it is difficult to classify every symptom and sign reported by an elderly patient as solely due to normal aging or due to
common pathologies associated with aging. This classification is further clouded by ageism in society. For example, loss of muscle mass is always noted as a consequence of aging, yet in one patient it may be due to lack of exercise and resistance training, in another due to lack of adequate vitamin D and protein intake, and in yet another due to caregivers who tell the patient he or she should not be exercising because of age. Which of these causes is normal? Which one requires an intervention? Medical models tend to focus on treating and preventing diseases that are commonly associated with aging. In some gerontological circles there is interest in identifying strategies to delay the overall effects of aging. This could aid in successfully treating all diseases because, currently, increased age is one of the most powerful risk factors for developing many disease states such as hypertension, diabetes, and cancer.

**Anti-Aging Strategies**

Many adults experiment with different strategies to reduce the effects of aging. Although no specific therapies have been proven effective in reducing the overall effects of aging, several potential strategies may eventually show results. One such treatment is calorie restriction, which focuses on reducing caloric intake by 30% to 40% of the normal amount for an average person of similar body type, while maintaining good nutritional balance. Animal models of yeast, worms, flies, rodents, and dogs have proven this method to extend life, but, to date, only observational studies have been completed in humans.

Antioxidant therapy using vitamin E, vitamin C, or coenzyme Q10 is frequently used based on the oxidative stress theory of aging. No studies have used these compounds to reduce aging or overall mortality, but several studies have attempted to reduce cardiovascular or central nervous system disease progression through supplementation of these antioxidants without success.

Replacement of estrogen, testosterone, DHEA, and human growth hormone have been touted as compounds that may reverse aging processes. Estrogen therapy in post-menopausal women did not prove effective in reducing cardiovascular disease or Alzheimer disease. Testosterone therapy has been tried in older men with low normal serum concentrations over 6 months and the results were significant improvements in fat and lean body mass, providing hope that this may prove to be a successful therapy in men. Although the exact role of DHEA in the body is not yet clear, clinical trials evaluating the supplementation of DHEA in older individuals with low concentrations showed a slight increase in bone mineral density, increased lean body mass, and an increase in perception of physical and psychological well-being. Because these results were not consistent across all studies, routine use of DHEA is not yet recommended.

Studies in adults with growth hormone deficiency show a reversal of catabolism, but studies with growth hormone as an anti-aging therapy did not add any benefit beyond that seen with resistance exercise training. Access to growth hormone in the United States has been limited by Congress to conserve supplies for individuals with genuine diagnoses known to respond to its administration, such as severe short stature syndrome in children and adult growth hormone deficiency. In spite of the lack of data, worldwide sales range from $1.5 to $2 billion, with at least one-third of this use for the off-label indication of aging prevention.

Resveratrol is a compound found in red grape skins, blueberries, and lingonberries that is thought to activate genetically controlled enzyme production of sirtuins in the body. Sirtuins regulate cellular reaction to stress and may help to prevent cancer, reduce cardiovascular disease, and extend life. Studies in yeast, fruit flies, nematodes, and fish have shown that resveratrol, presumably through sirtuin activation, can effectively extend the lifespan. It is thought that this compound may explain the French paradox, in which a low risk of heart disease is seen in France although the population consumes a diet high in saturated fats. Prospective controlled studies in humans with resveratrol have not yet been performed.
Other interventions focus on successful aging rather than promotion of longevity. Physical activity, cognitive stimulation, social engagement, and meditation are under research to evaluate their effects on cognitive and emotional aging.28

**KEY POINT:** Mankind has searched for the fountain of youth since the time of the Egyptian civilization. With the large variability in human genetic make-up, coupled with environmental exposures, no one factor can be expected to halt the aging process.

### Risk Factors for Functional Decline

Older adults report activity limitations more often than younger adults due to chronic medical conditions. Figure 3-1 shows how more medical conditions are reported as limiting activities in the youngest old, middle old, and oldest old. Of particular interest is the increase of senility and vision changes across these decades, such that they become the third and fourth most common reasons cited as limiting activity, behind arthritis/musculoskeletal and heart/circulatory conditions.38 Activity is defined as work or everyday household chores.

Functional decline in older persons is commonly described as a loss of independence in their ability to take care of themselves. Initially, this is evaluated by observing a person’s ability to perform activities such as shopping, housekeeping, preparing meals, taking medications, handling finances, and using public transportation (the instrumental activities of daily living). As disability increases, functional decline may occur with personal care, such as bathing and dressing (the activities of daily living). Functional decline generally results in a reduced quality of life, and the elderly patient who experiences progressive disability will exhaust functional reserves and become more vulnerable to adverse outcomes, including adverse drug events. Functional decline can result from physical issues, medical problems, cognitive changes, or a combination of these factors (see Table 3-2).39,40 Hospitalization is frequently a time when the diminished reserve capacity of the elderly patient contributes to a rapid decline in functional abilities. The patient is frequently confined to bed in an unfamiliar environment and given multiple treatments and medications.

### Table 3-2. Risk Factors for Functional Decline

<table>
<thead>
<tr>
<th>Physical</th>
</tr>
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<tbody>
<tr>
<td>Age</td>
</tr>
<tr>
<td>Immobility</td>
</tr>
<tr>
<td>Muscle strength</td>
</tr>
<tr>
<td>Exercise tolerance</td>
</tr>
<tr>
<td>Decreased balance</td>
</tr>
<tr>
<td>Undernutrition</td>
</tr>
<tr>
<td>Weight loss</td>
</tr>
<tr>
<td>Diminished lean body mass</td>
</tr>
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</table>

<table>
<thead>
<tr>
<th>Medical</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hospitalization and length of stay</td>
</tr>
<tr>
<td>Morbidity and disability from acute and chronic disease</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Psychological</th>
</tr>
</thead>
<tbody>
<tr>
<td>Impaired cognition</td>
</tr>
<tr>
<td>Depression</td>
</tr>
</tbody>
</table>

Medications can contribute to functional decline through multiple mechanisms. Mobility can be reduced with medications such as metoclopramide and antipsychotic agents if a patient develops secondary parkinsonism symptoms from their administration. Steroids and statins can contribute to muscle weakness, as can loop diuretics, which may cause hypocalcemia. Drugs that alter mental status including benzodiazepines, opioids, and anticholinergics reduce an elderly person’s ability to interact with others and the environment. Two of the most underappreciated drug side effects in older adults are anorexia and dysgeusia. Elderly patients, especially the frail elderly patient, frequently have weight loss, undernutrition, and a decrease in muscle mass. Use of medications such as digoxin, capto-
Frailty is an age-related increased vulnerability that has been shown to contribute to functional decline. Loss of physiological reserve capacity in the interrelated systems of the brain, skeletal muscle, endocrine system, immune system, and/or others place the geriatric patient at risk for a larger decline in functional abilities when a stressor occurs and, subsequently, an increased difficulty in regaining functional ability back to the pre-stress level. Generally, deficits in physical function, gait speed, and cognition are indicators of frailty, although older studies focus on activities of daily living and weight loss. Frailty prevalence increases from 4% in the young old, 16% in those 80–84 years old, and 26% in subjects over 85. Increased risk of falls, worsening disability, hospitalization, long-term care admission, and mortality with intermediate and severe levels of frailty have been shown in four large prospective cohort studies.
Age-Related Changes in Medication Sensitivity

Over one-third of prescription medications are taken by patients over the age of 65, even though this group makes up only 13% of the United States population. Although most of this medication use results in improvements in morbidity and mortality, a significant proportion of elderly patients experience adverse drug events. One study in over 30,000 geriatric outpatients found that 27.6% of adverse drug events were preventable, and that 42.2% of preventable adverse events were serious, life-threatening, or fatal.

Another study identified that 28% of hospital admissions in the elderly were attributable to adverse drug events. Use of medications in the elderly is one of the most challenging aspects of their healthcare. Important physiologic changes influence the pharmacokinetics and pharmacodynamics of medication use in older patients. A thorough understanding of these alterations will aid in optimizing pharmacotherapy and preventing adverse drug events in this vulnerable group of patients.

Age-Related Changes in Pharmacokinetics

Absorption

Most medications are absorbed in the small intestine through passive diffusion. Oral absorption of medications in the elderly patient can be delayed due to the slowing of transit time into the small intestine with no change in the overall absorption. Therefore, with chronic administration, this change makes little difference. A medication administered for an acute illness or symptom, such as pain, will take longer to reach the time to maximal concentration, have a lower maximal concentration, and have a slowed onset of action. The assessment of medication effectiveness should be delayed appropriately in this situation.

A subset of elderly patients may have achlorhydria, with decreased secretion of hydrochloric acid. This most often occurs in individuals with a history of peptic ulcer disease and/or gastric surgery. Treatment with high doses of proton pump inhibitors and histamine H2 blockers may also contribute. Patients with achlorhydria may have reduced absorption of vitamin B12, iron, and calcium.

Little evidence is available to identify whether significant changes occur with absorption of medications from transdermal patches. Changes in the skin associated with aging, such as reduced blood flow and thinner skin, should not be dismissed as possible enhancers or detractors of drug absorption through the skin. Studies with fentanyl transdermal patches in the elderly did not show statistically significant differences; however, great variability in absorption in all individuals may make such studies difficult to interpret. It is known that elevated body temperature will increase fentanyl absorption. The cooler skin of the elderly may likewise inhibit absorption.

Distribution

The distribution of medication throughout the body occurs through the bloodstream. The relative decrease in total body water, lean muscle mass, and the increase in percentage of body fat typically seen with older adults will alter the usual volume of distribution seen with medications. Water-soluble medications will have a smaller volume of distribution; therefore, smaller doses are required to attain a therapeutic response. If given the same dose as a younger adult, the older patient will have a higher serum concentration and be at risk for an increase in toxic effects. Aminoglycoside antibiotics are an example of a hydrophilic medication that exhibits a smaller volume of distribution in older patients with decreased total body water. Similarly, drugs that distribute into lean muscle mass will also have a smaller volume of distribution, and smaller doses should be used in the elderly. Digoxin has an average volume of distribution of 6–7 L/kg in young adults, but this average volume of distribution decreases to an average of 3–4 L/kg in geriatric patients.
Lipophilic medications pose a unique problem in the older patient. With the increase in the percentage of body fat seen with most geriatric patients, one would anticipate that a larger dose of a fat-soluble medication would be needed to fill up the larger volume of distribution. However, because the clearance of a medication is directly related to its volume of distribution, the geriatric patient will not be able to clear fat-soluble medications as quickly as a younger patient. These medications will accumulate, creating an increase in toxic effects. The following equation illustrates this relationship: 

\[
\text{Elimination half-life (t½)} = \frac{0.693 \times \text{volume of distribution}}{\text{clearance}}
\]

As the volume of distribution increases with the elimination half-life held constant, it will take longer to clear the medication from the body. To avoid this problem, lipophilic medications should be used at reduced doses or increased dosing intervals. Benzodiazepines and antipsychotic medications are examples of medications that are lipophilic but have a high risk for accumulation in the elderly patient due to the larger volume of distribution.

KEY POINT: The influence of the volume of distribution on the clearance of medications is overlooked in many package inserts, which report no difference in elimination between young adults and geriatric subjects.

Protein binding in the elderly patient may or may not be changed. Healthy older adults will have normal concentrations of albumin, alpha-1-acid glycoprotein, and other proteins. However, malnutrition and frailty are associated with lower serum proteins, particularly of albumin. If a drug is highly protein bound, it will be unable to find sufficient binding sites in the serum and more unbound drug will be available to exert pharmacologic (and toxic) effects, although its total serum concentration will still be within the therapeutic range. Phenytoin and warfarin are 99% protein bound, primarily to albumin. Their toxicity is increased in patients with hypoalbuminemia when the total serum concentration is within the therapeutic range because of the elevated free drug fraction in the serum.

**Metabolism**

The smaller size and lower blood flow through the liver have one important effect on drug dosing in the elderly patient. Because of these changes, drugs with high extraction during the first pass through the liver must be dosed cautiously. Less drug will be metabolized during the first pass through the liver, and the drug will have a higher bioavailability in the elderly patient. Verapamil, propranolol, and morphine are examples of medications that have a higher bioavailability in the older adult.

Researchers have never studied metabolic capacity in young or middle-aged adults and then re-studied the same group of subjects after they had aged to over 65 years, so it is still not clear what the exact effect of aging alone may be on the various metabolic pathways. Cross-sectional comparisons have shown a decrease in the function of CYP2C19, no change in CYP2D6, and a large variability in other isoenzymes. Because of the wide inter-individual variations in metabolism that exist for all age groups, we cannot be sure that all families of the CYP450 system are diminished with aging. Esterase activity was reduced in one study of frail elderly subjects but was not reduced in healthy elderly subjects. Cautious clinicians anticipate a decline in all Phase I reactions, oxidation, reduction, and hydrolysis, for elderly patients when dosing medications that are metabolized through these pathways. Phase II reactions, including glucuronidation, acetylation, and sulfation, have not shown a significant decrease in older adults. Medications which are metabolized through these pathways do not require adjustment.

Drug metabolism also occurs in the small intestine, renal cells, and lymphocytic cells through CYP3A4 enzymes or P-glycoprotein; however, studies show decreasing, increasing, or no change in activity.
Elimination

Although changes in liver metabolism are not completely understood, the reduced excretion of drugs through the kidneys is very well characterized for elderly patients. With age, renal mass and blood flow are reduced, with a correlated drop in the functioning glomeruli. Although not every older patient has abnormal renal function, longitudinal studies indicate that the glomerular filtration rate (GFR) drops on average by 1% for every year of age past 20, so that the oldest old who have survived six decades since their twentieth birthday will very likely have GFRs of <59 mL/min. Direct measurement of the GFR requires a 24-hour urine collection, which is inconvenient and time consuming for the patient, so most clinicians use an equation to estimate GFR or creatinine clearance, a closely related approximation of GFR, to evaluate a patient's renal function. The Cockcroft-Gault equation for estimating creatinine clearance is best validated for use in patients over 75 years of age and has the most data for drug dosing adjustments. This equation is:

\[
\frac{[(140 - \text{age in years}) \times \text{(body weight in kg)}]}{[72] \times \text{(serum creatinine in mg/dL)}} \times 0.85 \text{ for women}
\]

For individuals more than 30% over their ideal body weight, it is appropriate to use their ideal body weight.

Controversy surrounds the application of this as well as other estimates of renal function in the dosing of medications. One comparison of the Cockcroft-Gault formula with the Modification of Diet in Renal Disease (MDRD) and the Chronic Kidney Disease Epidemiology Collaboration formulas to estimate GFR in older adults identified that the latter two formulas significantly overestimated renal function such that drug overdosing errors would occur in patients with mild to moderate renal function. The investigators recommended use of the Cockcroft-Gault formula for drug dosing. Individuals with low muscle mass generally have low serum creatinine concentrations. This gives rise to an over-estimate of kidney function when serum creatinine values below 0.8 mg/dL are used in the formula. Many clinicians advocate rounding extremely low serum creatinine values upward; however, studies have not supported this practice.

The kidney also functions to secrete molecules in the tubules of the nephrons and to metabolize certain compounds. Both functions are reduced with aging. Tubular secretion is reduced in proportion to the reduction in nephrons with a smaller kidney size. Approximately 10% of creatinine elimination is through tubular secretion rather than through filtration by the glomeruli; therefore, formulas for estimating creatinine clearance may not adequately account for this mode of elimination. Certain medications can inhibit the secretion of creatinine or other medications by the tubules. Trimethoprim and cimetidine are drugs that compete with creatinine for tubular secretion, so individuals receiving these agents may have an elevated serum creatinine that does not correctly reflect their level of renal dysfunction. Metabolism of insulin occurs in the renal cells, so with reduced numbers of functioning cells a reduction in clearance will occur. Elderly patients with very poor renal function will experience an extended half-life of all insulin products such that regular insulin may exert effects lasting as long as a long-acting form of insulin would in a younger adult. Finally, activation of vitamin D occurs in the kidney, with metabolism of 25-hydroxy-vitamin D3 to 1, 25-di-hydroxy-vitamin D3. But in the elderly patient with reduced kidney function, this activation does not occur at the rate necessary for calcium homeostasis. Many elderly patients are deficient in activated vitamin D, with resulting hypocalcemia and subsequent hyperparathyroidism.

Although several important drugs are excreted through the biliary tree, no significant alterations in clearance associated with aging have been identified.

Age-Related Changes in Pharmacodynamics

The cardiovascular system is frequently associated with pharmacodynamic changes in the elderly patient. This is partially because medi-
Cations affecting the cardiovascular system are frequently used in the elderly patient. As the catecholamine level increases, down-regulation of cardiac beta-1-adrenergic receptors occurs that leads to a blunting of effect of antagonist agents such as metoprolol.\textsuperscript{11} The risk for orthostatic hypotension due to antihypertensive agents is increased in older patients.\textsuperscript{22} The diminished capacity of the baroreceptors to react to the drop in blood pressure with rising is one cause of this increased risk. In addition, the presence of isolated systolic hypertension accentuates the magnitude of the blood pressure drop. An increased sensitivity to medications that prolong the QT interval is seen, raising the risk for torsades de pointes.\textsuperscript{56}

Table 3-3 summarizes other sometimes unexplained alterations in pharmacodynamic sensitivity to medications and includes specific recommendations to reduce the risk for adverse events.

<table>
<thead>
<tr>
<th>Table 3-3. Pharmacodynamic Changes and Recommendations</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Start with very low doses of beta-adrenergic blockers and calcium channel blockers and titrate up slowly to avoid hypotension and bradycardia.</td>
</tr>
<tr>
<td>2. Avoid use of tricyclic antidepressants, antipsychotics, diuretics, angiotensin-converting enzyme inhibitors, alpha-adrenergic blockers, dopamine agonists, direct vasodilators, and opioids to minimize orthostatic hypotension.</td>
</tr>
<tr>
<td>3. Closely monitor use of diuretics and angiotensin-converting enzyme inhibitors for fluid and electrolyte abnormalities and changes in oral intake of fluids, especially with emesis or diarrhea.</td>
</tr>
<tr>
<td>4. Avoid combining medications that prolong the QT interval.</td>
</tr>
<tr>
<td>5. Start with very low doses of benzodiazepines and choose lorazepam or oxazepam because of their hydrophilic properties and Phase II metabolism.</td>
</tr>
<tr>
<td>6. Avoid drugs with anticholinergic properties. Even minor amounts of anticholinergic effect, if present in multiple medications in the patient’s regimen, may be additive.</td>
</tr>
<tr>
<td>7. Begin with lower doses of warfarin to avoid the risk for overshooting the therapeutic INR range.</td>
</tr>
<tr>
<td>8. Anticipate a therapeutic response to anticonvulsants and immunosuppressants at the lower end of the therapeutic range.</td>
</tr>
<tr>
<td>9. Anticipate gastrointestinal hemorrhage from nonsteroidal anti-inflammatory agents due to increased susceptibility.</td>
</tr>
<tr>
<td>10. Use a two-step tuberculosis skin test because of a decreased responsiveness in the elderly patients, particularly those residing in long-term care facilities.</td>
</tr>
</tbody>
</table>

INR, international normalized ratio.
Case: Emergency Department

Setting:
Acute care hospital emergency department.

Subjective:
DH is a 79-year-old man who presents to the hospital with swelling and tenderness of his right lower extremity.

Past Medical History:
Atrial fibrillation, congestive heart failure, chronic kidney disease (baseline serum creatinine of 1.4 mg/dL 4 months ago), neuropathic pain.

Medications:
Furosemide 20 mg daily, fosinopril 40 mg twice daily, spironolactone 25 mg daily, metoprolol XL 25 mg daily, gabapentin 300 mg TID as needed for pain.

Allergies:
Penicillin caused “breathing problems.”

Social History:
Retired engineer; lives with his wife.

Family History:
Noncontributory.

Objective:
Ht 66”, Wt 136.6 lb, BP 132/80 mmHg, P 89 BPM, RR 15/min

Physical Examination:
Within normal limits except heart with irregularly irregular rhythm and right lower extremity with macular erythematous rash over right shin, pain to palpation, and 4+ pitting edema.

Labs:
Complete blood count within normal limits except white blood count 16 × 10³ mm³ with 93.9% granulocytes, hemoglobin 10.2 g/dL, hematocrit 32.6%; electrolytes within normal limits. BUN 55 mg/dL, serum creatinine 3.7 mg/dL; PT 14.9 seconds, INR 1.2, PTT 26.9 seconds.

Assessment:
DH is a 79-year-old man with possible cellulitis.

Plan:
Admit to hospital, draw blood cultures, and begin vancomycin 1 g every 24 hours for cellulitis. Check trough vancomycin level for further dosing adjustment and monitor BUN, serum creatinine, white blood cell count, and physical findings. Dosing adjustment for other renally eliminated medications. Evaluate patient for etiology of anemia and initiation of warfarin to prevent stroke.
Rationale:

1. Usual vancomycin dosage recommendations are 15–20 mg/kg/dose given every 12 hours in patients without renal insufficiency. The dose range for DH calculates as 930 mg to 1240 mg. Since 1000 mg is within this range and is a typical dose, it should be selected. DH weighs 62 kg, which is 1.8 kg below his calculated ideal body weight, so his actual weight should be used to calculate his creatinine clearance; this calculation is 14 mL/min estimated by the Cockcroft-Gault equation. With this degree of renal insufficiency, vancomycin (a renally eliminated drug) will accumulate if dosed at the usual adult dosing range, so an extended interval is indicated. Drug information resources recommend every 24 hours or more.

2. Although the assessment does not mention that DH is dehydrated, the elevated BUN supports this possibility. A vancomycin trough level will guide further dosing more specifically regardless of the serum creatinine; hence, the creatinine clearance calculation increases or decreases. The white cell count and physical findings will provide evidence of response to the antibiotic therapy.

3. The gabapentin dose for DH should be evaluated, as it is renally eliminated. At a creatinine clearance of 14 mL/min, resources recommend a maximum dose of 300 mg daily. Furthermore, DH has a significant anemia, and his hemoglobin may decrease further with hydration. His anemia should be evaluated and appropriate therapy instituted. Finally, his records should be reviewed to identify why he is not anticoagulated to prevent embolism secondary to atrial fibrillation. If contraindications are not identified, warfarin should be added to his regimen.
Clinical Pearl

• The most famous adage about pharmacotherapy for geriatric patients is *Start low, and go slow!* When we start low, the changes in the volume of distribution, protein binding, and pharmacodynamics of an elderly patient are addressed. When we go slow, the changes in metabolism and excretion are handled.

**Chapter Summary**

Pharmacotherapy is one of the most challenging aspects of geriatric care because of age-related biologic changes. Although many physiologic changes are common, few changes are due to aging itself. The impact that these changes have on the pharmacokinetics and pharmacodynamics of medications used to treat the older adult must be recognized in order to provide optimal pharmaceutical care. The pharmacist and other healthcare providers must apply these principles to avoid causing drug-related problems. As more is understood about the process of aging, more opportunities will arise to ensure that each patient has the tools needed to age successfully.

**Self-Assessment Questions**

1. What observational and interventional trials support or refute the most popular theories of aging, such as damage theories and programmed theories?
2. Which cardiovascular changes in older adults are part of the normal aging process, and which changes are more likely characterized as common in patients over the age of 65?
3. What are the expected changes seen in cognition as one grows older, and how do they compare with changes seen in patients diagnosed with dementia?
4. What are the components of successful aging? How do they differ according to perspective?
5. Which anti-aging therapies have been tested in humans, and what are the results?
6. How do the changes associated with aging seen with lean body mass and body fat affect the volume of distribution of hydrophilic and lipophilic medications?
7. What would be the pharmacokinetic characteristics of the ideal drug for use with older patients?
8. What changes occur in Phase I metabolism as compared to Phase II metabolism in elderly patients?
9. Why are the changes in pharmacodynamics important to consider when choosing and dosing a medication for an elderly patient?

**References**


Learning Objectives

1. Describe standard physical assessments necessary in geriatric patients.
2. Compare and contrast mood, behavioral, cognitive, and functional assessments commonly utilized in clinical practice and research settings.
3. Describe important social assessments that should be performed in geriatric patients.
4. Explain changes that might be necessary for performing assessments in institutionalized patients and those with cognitive impairment.

Key Terms and Definitions

**ADL:** Activities of daily living, such as bathing, dressing, and feeding.

**ADVANCE DIRECTIVES:** Legal documents that allow patients to have their medical decisions known and followed when receiving care.

**GDS:** Geriatric depression scale, a tool specifically for geriatric patients to screen for depression.

**IADL:** Instrumental activities of daily living, such as shopping, paying bills, and managing medications.

**MMSE:** Mini-mental state examination, a tool commonly used in screening for cognitive impairment.

**NPI-Q:** Neuropsychiatric inventory questionnaire, a tool used in clinical practice to help with assessing neuropsychiatric symptoms of dementia.

**TUG:** Timed “up and go” test, used to assess balance and fall risk in the elderly.
**Introduction**

Due to the complexity of geriatric patients, assessment by healthcare providers typically requires more extensive investigation than for younger adults and may involve multiple healthcare practitioners. Furthermore, the frail elderly patient frequently presents with symptoms that are atypical for a specific disease. This makes diagnosis, treatment, and monitoring a challenge. A full assessment should include physical assessment and laboratory tests, a review of medical problems and medications, cognitive assessment, neuropsychiatric assessments, functional assessment, and social assessments. In addition to the evaluation of current medical problems, screening for diseases or conditions and plans for health promotion and disease prevention are also likely to be included when assessing relatively healthy elderly patients. Health promotion in the form of testing, diagnosing, and treating may be omitted in patients where life expectancy is not likely long enough to receive benefit from the intervention (e.g., lag time to benefit is longer than life expectancy).

Caregivers, children, the medical power of attorney, and other individuals involved in the care for geriatric patients should be included in visits, if feasible, to assist in reviewing medical information about the patient. Typically, more than one visit is required to complete a comprehensive assessment of geriatric patients. It is also important to note that changes in the geriatric assessment may be required in those who are institutionalized or have cognitive impairment. Overall, the geriatric assessment should be tailored to the individual patients, based on their age, frailty, and living situation and, whenever possible, should include assessments from interprofessional team members and caregivers.

Interprofessional team members who may be involved in assessing geriatric patients include physicians, nurse practitioners, physician assistants, nurses, pharmacists, social workers, physical therapists, occupational therapists, neuropsychologists, dentists, and nursing aides and assistants. Although pharmacists can be involved in every step of the geriatric assessment, the most critical place for pharmacists to take an active role is in the assessment of medications and medication-related problems. Pharmacists are uniquely trained to identify drug therapy problems and to make recommendations regarding drug therapy, immunizations, and adherence. Capitalizing on the individual strengths of the geriatric interprofessional team members, including the pharmacist, allows for a more comprehensive assessment.

The purpose of this chapter is to discuss in detail the steps involved in a comprehensive assessment of a geriatric patient and to underscore the importance of the assessment in the overall treatment plan for the patient.

**KEY POINT:** The geriatric assessment should be tailored to the individual patient, based on his or her age, frailty, and living situation.

**Physical Assessment and Laboratory Evaluation**

Physical assessment in the elderly involves elements typically performed in younger adults, with additions based specifically on the likelihood of chronic disease states, such as diabetes, chronic kidney disease, dementia, and depression. Physical assessment for a new patient should include review of all systems, vital signs, and examination of the eyes, skin, lungs, cardiovascular system, head and neck, musculoskeletal system, abdomen, and neurologic system. Many of the additional assessments necessary in elderly patients evaluate for the presence or consequences of chronic diseases.

Of note, the physical assessments and laboratory evaluations described below are for healthy elderly patients and may need to be altered or...
eliminated in frail elderly patients, depending on the patient’s goals for care and life expectancy. Acute illness in frail patients is often atypical and, therefore, requires very careful assessment to avoid underdiagnosis, overdiagnosis, or misdiagnosis. Specific aspects of these challenges are discussed in the organ system chapters, but it is important to remember that incomplete or suboptimal assessment in these individuals may not only lead to inaccurate diagnosis but, subsequently, to inappropriate medication therapy.

**Vital Signs**

Typical vital signs (blood pressure, pulse, temperature, respiratory rate, and level of pain) are standard measurements necessary for a medical assessment in the elderly, and for the most part they can easily be performed by a pharmacist. In the elderly, pain is especially important to evaluate because of the high incidence of osteoarthritis and chronic pain and often needs investigation beyond a pain score. At a minimum, patients should also be evaluated for the location and type of pain they are experiencing. Blood pressure measurements in the elderly must be done with care. For example, it is important to select the correct size cuff (e.g., small, regular, or large) and to inflate it sufficiently to make sure the correct systolic measurement is taken. An auscultatory gap is a common phenomenon among older patients with hypertension, so care must be taken to avoid a falsely low systolic measurement. This can be achieved by inflating the cuff to approximately 200 mmHg. Because this may be uncomfortable for some patients, one can palpate the radial pulse prior to assessing blood pressure and then inflate the cuff at least to the point where this radial pulse can no longer be detected, rather than routinely inflating to 200 mmHg. Orthostatic blood pressure measurements may also need to be evaluated due to aging, disease, and drug-related causes of orthostatic hypotension. Heart rate should also be assessed when performing orthostatic hypotension assessments to aid in the differentiation between orthostasis and syncope. When assessing the pulse, it is important to note whether the patient has a regular or irregular rhythm. As a standard vital sign, temperature should be checked at all visits. Any elevated temperature in the elderly is worrisome and should not be disregarded. Repeated temperature measurements greater than 99°F on two or more occasions, or an increase in temperature of more than 2°F above baseline, usually indicate fever in an elderly patient.

Patients with clinical signs or symptoms of infection but with normal oral or tympanic temperatures should have a rectal temperature measurement performed, as it can be more accurate in elderly patients. Height and weight should be measured at the first visit, and weight should be measured at all future visits. Weight and appetite should be evaluated to assess whether the patient is under- or overweight. Both obesity and malnutrition occur in the elderly, but in the very elderly malnutrition is more common. Multiple studies indicate that older adults who are undernourished have increased morbidity and mortality. If the patient is obese, undernourished, or underweight, an intervention should be made. Referral to a dietitian for nutrition counseling, a speech-language pathologist for a swallow study, or a dentist for an oral evaluation can be helpful in patients with malnutrition. The United States Preventive Services Task Force (USPSTF) recommends that all adults be screened for obesity utilizing a body mass index (BMI) calculation, with multicomponent behavioral interventions offered to anyone found to be obese (e.g., BMI > 30 kg/m²). Measured height can be compared with patient-reported height to help identify whether the patient may have vertebral fractures. If the patient is unable to get out of bed or has significant kyphosis, height can be estimated using knee height, forearm length, total arm length, or demi-span (the distance from the middle of the sternal notch to the tip of the middle finger).

**Ophthalmic, Otoscopic, and Oral Assessments**

Eye examinations in the elderly should be performed by an optometrist at least annually. With increasing age, vision can deteriorate, and
there is an increased risk for ophthalmic disorders, such as glaucoma, macular degeneration, cataracts, and diabetic retinopathy. If driving, the patient should be assessed for the ability to see well enough to drive an automobile. In some states a driver’s license lasts for 10–20 years; during the time that the license is still active, vision changes can occur that cause problems when driving. To prevent accidents in the home or automobile, it is important to reassess vision periodically even if the patient is not complaining of vision changes. Also, the patient may need referral to an ophthalmologist if the optometrist cannot fully assess the patient or he or she has complications of an ophthalmic disorder.

Ear examinations are also necessary in the elderly, as many may have hearing loss. Ears should be examined specifically for impacted cerumen, which is often due to dry cerumen and/or the use of hearing aids. The inability to hear can have negative consequences in the elderly, such as the appearance of cognitive impairment and low health literacy. In addition, impacted cerumen can make patients dizzy, predisposing them to falls. Hearing tests by an audiologist and further use of corrective hearing aids may improve quality of life. In patients with dementia, a finger rub or finger friction test can be utilized to assess hearing and has been shown to have high sensitivity and specificity compared to audiometry. Microphones with connected headsets (e.g., Pocket Talker) can also be used by healthcare practitioners to improve communication with patients who have hearing impairment.

Oral problems often contribute to malnutrition in the elderly patient. Both medical providers and dentists can evaluate elderly patients for dryness, but dentists are better suited to evaluate for the number of teeth present, denture fit (if applicable), the ability to chew food, and the presence of dental caries and oral cancers. If xerostomia is present, pharmacists can work with dentists and medical providers to reduce drug causes of xerostomia.

**Skin Assessment**

Skin examinations in the elderly should focus on dryness, cellulitis, edema, and cancer. Due to impaired sensation in the skin and impaired vision, elderly patients may not realize that their skin is dry, damaged, or infected. This is especially true for patients with diabetes, who often suffer from neuropathies in their extremities, as their sensation may be diminished and their report inaccurate. Edema is more prevalent in patients with heart failure but can also occur as a side effect of medications or just poor circulation. In addition to a skin and extremities examination, weight can also be used to help determine how much fluid overload is present.

**Pulmonary Assessment**

Lung examinations in the elderly are similar to those in younger patients, taking into account that those with kyphosis may require a more meticulous assessment. If a patient has heart failure, the lung examination may also include an assessment for pulmonary edema (e.g., rales). Pulmonary function tests are also helpful to evaluate the severity of asthma and chronic obstructive lung disease. Patients may also be candidates for further testing with a sputum test, chest x-ray, or computed tomography (CT) to screen for lung cancer if they meet the following characteristics: (1) their age is less than 75–80 years, (2) they have at least a 30 pack-year smoking history, (3) they are currently smoking or stopped within the past 15 years, or (4) they are in fairly good health and/or are able and willing to have curative lung surgery if cancer is detected.

**Cardiovascular Assessment**

Cardiovascular examinations should evaluate patients for murmurs and arrhythmias, such as atrial fibrillation. Blood pressure (both regular and orthostatic) as indicated above should be assessed and evaluated, recording time of day and corresponding heart rate. Based on the patient goals, for a patient with hypertension a fasting lipid panel should also be performed to evaluate whether he or she has dyslipidemia.
the patient has a sustained blood pressure of at least 135/80 mmHg, the USPSTF recommends screening the patient for type 2 diabetes every 3 years, typically using a fasting plasma glucose concentration or an HbA1c measurement. An electrocardiogram, carotid auscultation, and an echocardiogram may also be needed to further evaluate for arrhythmias, stroke risk, and heart failure, respectively. If the patient has a history of cardiovascular disease or cardiac risk factors, he or she should also be evaluated for peripheral vascular disease (PVD) with the ankle-brachial index. This simple calculation divides the systolic blood pressure in the ankle/foot by the systolic blood pressure in the arm to determine the index. A quotient below 0.8 is considered positive for PVD.

Musculoskeletal Assessment

Musculoskeletal examination in the elderly should evaluate range of motion in the joints; stability; strength; and the ability to rise from a sitting position, stand, bend forward, bend down, walk, and rotate the head around naturally. A proper amount of space is required to evaluate the patient. Some gait changes occur naturally with aging, such as narrowing or widening of the stance. Gait and balance will also be discussed further (see Functional Assessment).

Abdominal and Urologic Assessment

Palpation of the abdomen in the elderly is important to identify any masses and hernias. In this population, abdominal examinations often elicit a history of constipation, which is common because of the adverse effects of medications, decreased water and fiber intake, and lack of activity. A rectal examination may identify hemorrhoids and/or an enlarged prostate in men. Prostate cancer screening with a prostate-specific antigen (PSA) blood test is extremely controversial and is no longer recommended by the USPSTF. The American Cancer Society recommends that providers discuss screening in men with a life expectancy of at least 10 years. An evaluation for colon cancer (such as a colonoscopy) every 10 years, a flexible sigmoidoscopy every 5 years, a double contrast barium enema every 5 years, or a CT colonography every 5 years should also be offered. Due to the invasiveness of colon cancer screening procedures and the lag time to benefit of approximately 10 years, there is no agreement about how long to continue testing. The USPSTF recommends stopping screening at 75 years of age, but regardless of age, if a patient is frail and would choose not to treat a detected cancer, there is often no benefit to performing screening. Urologic examinations should focus on urinary retention, incontinence, and benign prostatic hypertrophy. Many clinics now have ultrasound machines that can evaluate post-void residuals in patients with urinary retention; this can also be done with a urinary catheter. Pap smears in women can be stopped at age 65 if patients have had regular cervical cancer screening with normal results or if they are otherwise not at high risk for cancer. However, the American Cancer Society recommends continuing testing for at least 20 years after diagnosis of any serious cervical pre-cancer. Elderly women should also be asked about symptoms of vaginal dryness.

Neurologic Assessment

Thorough neurologic examination in the elderly can identify many subtle abnormalities in muscle strength, sensation, reflexes, sensory motor skills, coordination, tremor, muscle tone, and postural stability. In a study of older, community-dwelling adults without overt neurological disease, multiple subtle neurologic abnormalities were associated with cognitive and functional decline and independently predicted mortality and cerebrovascular events. In addition, cognition should be evaluated either with the neurologic examination, or separately. A discussion of cognitive assessment is found later in this chapter.

Other Assessments

Other evaluations that should be done in the elderly include an assessment of sleep, and a foot examination to evaluate for pulses, dryness, nails, ulcers, and deformities. Patients with
foot abnormalities or functional deficits can be referred to a podiatrist for further evaluation. In addition, a clinical breast examination and mammography is recommended annually in women if they are in good health; and a dual-energy x-ray absorptiometry (DEXA) is recommended for all elderly women and high-risk men, to evaluate their bone mineral density for osteoporosis. The DEXA should be performed on all eligible patients as long as they are able to lay down comfortably during the procedure and are eligible for osteoporosis treatment. Medicare will cover one screening DEXA test every 2 years. Evaluating and assessing osteopenia or osteoporosis further can be facilitated by using the World Health Organization Fracture Risk Assessment Tool (FRAX) available online at http://www.shef.ac.uk/FRAX/. The tool takes into account patient-specific risk factors such as age, height, weight, race, country of origin, concomitant medications, disease states, and bone mineral density (if available) to estimate the 10-year probability of fracture. The tool can also be used to decide whether drug treatment is warranted based on the cost-effectiveness of treatment.

**Laboratory Measurements**

Typical baseline laboratory measurements that should be obtained in the elderly include thyroid stimulating hormone (TSH), complete blood count (CBC), and a basic metabolic panel to evaluate electrolytes and serum creatinine (Scr). In patients with a life expectancy of 3 years or more, a fasting lipid panel to screen for hypercholesterolemia may be indicated. Using the Scr, an estimation of creatinine clearance (CrCl) should be performed on all elderly patients at baseline and if the Scr increases significantly. Although it may underestimate the CrCl slightly, the Cockcroft-Gault equation is still preferred for use in the elderly to estimate kidney function and adjust medication doses, as discussed in Chapter 3.

Additional laboratory measurements are indicated in specific situations: an HbA1c if the patient is diabetic; vitamin B12 if the patient is malnourished or has memory loss, anemia, depression, fatigue, or neuropathy; serum drug concentrations for certain narrow therapeutic index drugs (e.g., digoxin, phenytoin); liver function tests if the patient is on medications that can raise these concentrations; and a serum 25-hydroxy vitamin D concentration, especially if the patient has a history of falls or osteoporosis, is obese, takes no vitamin D supplement, or is institutionalized. After laboratory tests have been measured once, Medicare may not reimburse for them again for a certain time period. For example, unless the patient has an indication such as hyperlipidemia, hypertension, or coronary disease, Medicare may not reimburse for another screening fasting lipid panel for 5 years. Medicare also has the restriction that HbA1c cannot be checked more often than once a month.

**KEY POINT:** The type and frequency of laboratory examinations in the elderly are often governed by Medicare’s reimbursement restrictions.

**Assessments in Those Who Cannot Provide a Self-Report**

Physical examination and review of systems in patients who cannot provide a self-report is often difficult and may rely on caregiver input. In patients who are institutionalized or who cannot provide a self-report, some examinations and screenings may be eliminated because the provider is limited to bedside assessments. Certain screenings may not be necessary. Generally, the risks and benefits of the examination/screening can be reviewed by the provider, patient, family, or medical power of attorney to help determine how aggressive or limited to make the examination. Vision and hearing assessment are typically only necessary for establishing a patient’s quality of life. However, if the patient is unable to respond, it is not always possible to get accurate results. Studies of pain assessment in elderly patients with cognitive impairment indicate that self-report pain scales can still be used. Based on
several studies, it appears that elderly persons with cognitive impairment respond reasonably well to the Verbal Rating Scale (none, mild, moderate, or severe), the Numeric Rating Scale (1–10 horizontal scale), and the FACES rating scale (utilizes facial expressions to rate pain).17-19 Other means of assessing pain may be necessary in nonverbal patients or those with severe cognitive impairment.

**Review of Medical Problems and Medications**

The medical history of a geriatric patient can be extremely complex and time consuming to elicit. Often, the patient may not have previous medical records and may not fully remember his or her medical history, so care must be taken to order pertinent medical records from previous providers and hospitals. A complete medical history should include a family history, history of present illness, active medical problems, past medical problems, past hospitalizations, and past surgical procedures. It is especially helpful to identify the dates because they can change current medical therapy. For example, if a patient had a coronary stent placed several years ago, it may be possible to reduce dual antiplatelet therapy, unlike a patient who had a coronary stent placed in the last several months. A functional health literacy assessment can also be performed to assess the patient's ability to obtain, process, and understand basic health information and make appropriate health decisions.20 Examples of formal assessments of health literacy include the Rapid Estimate of Adult Literacy in Medicine (REALM) and the Test of Functional Health Literacy in Adults (TOFHLA).21,22 The short forms of these assessments, along with the Newest Vital Sign (NVS), are quicker to administer and, therefore, may be more appropriate for clinical practice.23

A recent immunization history should be obtained for every elderly patient, as multiple immunizations are indicated for them. All patients should be evaluated for a history of pneumococcal vaccination, yearly influenza vaccinations, herpes zoster vaccination, and a tetanus/diphtheria (Td) or tetanus/diphtheria/acellular pertussis (Tdap) booster. Unvaccinated older adults can be referred to their local pharmacies for indicated immunizations.

A full medication assessment is also essential for geriatric patients. This should include current use of prescription drugs and over-the-counter (OTC) vitamins, supplements, and herbal medications. The patient's pharmacy contact information should be obtained as well. Past use of medications for chronic diseases, such as chronic pain, diabetes, and hypertension, can also be useful to optimize future therapy and to update the allergy/adverse event profile, if applicable. A pharmacist is well equipped to perform the medication assessment or provide valuable input. Special insight from the pharmacist can help to identify drugs with no medical indications, drugs treating side effects of other drugs, duplications in therapy, drug–drug and drug–disease interactions, adverse effects, inappropriate or inadequate prescribing, nonadherence, and other drug therapy problems.

Pharmacists are integral in reducing drug-related costs for elderly patients. This can be accomplished in many ways, but it typically includes increasing Medicare Part D formulary adherence to lower tier medications and recommendations for discontinuing medications. Pharmacists can also help patients utilize pharmacy-specific drug discount programs (e.g., $4 generics) and manufacturer patient assistance programs, and they can ensure that the patient applies for extra assistance from state or federal programs (e.g., Social Security extra assistance or Medicaid).

**KEY POINT:** Insight from the pharmacist can help identify drug therapy problems, opportunities for reducing drug-related costs, and the need for patient education.
Along with a functional health literacy assessment, it is helpful to assess understanding of medications and disease states. How skilled a patient is in the self-administration of medications should also be determined. If the patient cannot perform these duties, plans for assistance should be made. Simple devices, such as pillboxes or calendars, can help many elderly patients remember to take their medications. For those with cognitive impairment or complex medication regimens, family members or caregivers may have to assist with administration. Nonadherence in the elderly can be intentional (e.g., to save money or to prevent side effects) or unintentional (e.g., too complex for patient to handle or forgetting to order refills). For institutionalized patients, medication adherence cannot be assumed because patients still have the ability to refuse their oral medications and unforeseen circumstances may prevent administration. Specific tools, such as the Morisky Scale, the Drug Regimen Unassisted Grading Scale (DRUGS), and Medication Management Instrument for Deficiencies in the Elderly (MedMaIDE™) instruments, can assist the pharmacist in assessing the patient's capacity to manage medications, including adherence.24,25 The Morisky Scale consists of yes/no questions for patients to ascertain whether they are forgetting to take medication or are purposefully choosing to stop due to hassles or side effects. It has been adapted and validated for use in hypertension in seniors. The DRUGS evaluation involves asking patients about each of their own medications and comparing their responses to the medication directions, calculating a percentage of answers regarding naming the drug, identifying the correct directions, and identifying the time of day for administration. Poorer scores are associated with lower Mini-Mental State Examination (MMSE) scores and increased risk of institutionalization. The MedMaIDE™ instrument is designed to identify whether a patient understands what his or her medications are for, and how to obtain and administer them.

Pharmacists providing medication therapy management (MTM) services will typically perform a thorough medical, medication, and adherence assessment. Pharmacists directly working with the primary care provider may have access to the medical records for the patient, but pharmacists providing services from a community pharmacy setting or through the Medicare Part D plan may only have access to limited medical record information along with medical and drug claims data. Pharmacists seeing patients in person for MTM can perform their own vital signs to evaluate the patient's drug therapy. Overall, pharmacists have the knowledge and ability to make many recommendations for patients to optimize their medications, improve adherence, reduce drug costs, and prevent adverse drug events.

Pharmacists providing MTM services or seeing geriatric patients in the community may refer patients to a geriatrician for a more thorough medical review. Moreover, interprofessional teams are important for quality care for complex geriatric patients. Depending on the state in which they practice, pharmacists can directly refer patients to a physical therapist, occupational therapist, social worker, or dietitian for additional assistance with their healthcare, functioning, or social issues, although a physician's order may be necessary for Medicare to pay for the services.

**Cognitive Assessment**

Although the USPSTF concluded that evidence is insufficient to assess the balance of benefits and harms of cognitive screening, many clinicians prefer to screen for cognitive impairments in older adults. If cognitive screening is warranted, assessment should be performed at one of the first visits and then yearly, or as often as determined to be clinically relevant. There are multiple tools to assess cognition, but typically clinicians will utilize the MMSE, Mini-Cog, or the St. Louis University Mental Status (SLUMS) Examination.26-28 These tools are most utilized as they are quick to perform and are often reprinted for clinic use. They can be utilized in the outpa-
Pharmacists in many settings can easily initiate screening if they detect potential cognitive impairment, such as while performing MTM services or discussing adherence. In patients who may have complex cognitive impairment or for clinicians who are not comfortable with cognitive testing, referring patients to a neuropsychologist, speech-language pathologist, or neurologist trained in cognitive testing can be useful.

**KEY POINT:** There are multiple tools to assess cognition, but typically clinicians will utilize the Folstein Mini-Mental State Examination (MMSE), Mini-Cog, or the SLUMS Examination.

The MMSE is a widely used clinical tool for assessing cognitive impairment associated with dementia and is typically used to stage Alzheimer disease as mild, moderate, or severe. It includes 11 questions assessing five different domains: short-term memory (recall), orientation, attention, language, and short-term memory (retention). The maximum possible score for the test is 30 points. Typically, a score of 24–30 indicates a negative screen, 19–23 indicates mild deficits, 10–18 indicates moderate impairment, and less than 10 indicates severe cognitive impairment. The examination takes approximately 7–10 minutes to administer but possibly longer if the patient has more severe cognitive impairment. Some disadvantages of the MMSE are that education level and language barriers can influence the results. It is also copyrighted and must only be used with permission or for a fee. However, the MMSE has been translated into multiple languages, making it appropriate for use in a broad population of patients.

The Mini-Cog (Figure 4-1) is a combination three-item recall and a Clock Drawing Test (CDT). It is a simple, brief, and valid screening tool designed to identify individuals at high risk for dementia. Because the Mini-Cog takes approximately 3 minutes to administer, it is extremely simple for clinicians to remember and use. Moreover, pharmacists can easily implement the Mini-Cog into their assessments when discussing adherence, ability to self-administer medications, or medication management services. The Mini-Cog assesses short- and long-term memory, verbal comprehension, conceptualization, and executive functioning. It has a sensitivity of 76% to 99% and a specificity of 89% to 93% at detecting cognitive impairment.

Additional screening tests for cognition include the SLUMS Examination (Figure 4-2), the Seven Minute Screen (7MS), and the Montreal Cognitive Assessment (MoCA). The SLUMS is similar in format to the MMSE, with a 30-point, 11-item scale. Patients are scored based on their level of education and classified as normal, having mild neurocognitive disorder, or having dementia. The SLUMS examination is comparable to the MMSE at detecting cognitive impairment and appears to be possibly better at identifying mild neurocognitive disorder. Many clinic settings, along with most Veterans Affairs facilities, utilize the SLUMS examination because of its enhanced benefit in identifying mild cognitive disorders and lack of copyright issues. The 7MS is another neurocognitive screening tool developed to provide improved sensitivity. It is composed of four brief tests: orientation, enhanced cued recall, CDT, and verbal fluency. The 7MS administration time ranges from 6 to 11 minutes and has performed better than the MMSE at evaluating very mild to mild Alzheimer disease; also, it is not affected by gender, age, or education level. The MoCA examination was designed to detect mild cognitive impairment (MCI) and has been translated into many languages for use. It takes about 10 minutes to administer and assesses attention, concentration, executive functions, memory, language,
MINI-COG™

1) GET THE PATIENT’S ATTENTION, THEN SAY: “I am going to say three words that I want you to remember now and later. The words are Banana Sunrise Chair.

Please say them for me now.” (Give the patient three tries to repeat the words. If unable after three tries, go to next item.)

(Fold this page back at the TWO dotted lines BELOW to make a blank space and cover the memory words. Hand the patient a pencil or pen.)

2) SAY ALL THE FOLLOWING PHRASES IN THE ORDER INDICATED: “Please draw a clock in the space below. Start by drawing a large circle.” When this is done, say: “Put all the numbers in the circle.” When this is done, say: “Now set the hands to show 11:10 (10 past 11).” If subject has not finished clock drawing in 3 minutes, discontinue and ask for recall items.

-------------------------------------------------------------------------------------------------------------------------------

3) SAY: “What were the three words I asked you to remember?”

(Score 1 point for each) 3-Item Recall Score

Score the clock (see other side for instructions):

<table>
<thead>
<tr>
<th>Normal clock</th>
<th>2 points</th>
</tr>
</thead>
<tbody>
<tr>
<td>Abnormal clock</td>
<td>0 points</td>
</tr>
</tbody>
</table>

Total Score = 3-item recall + clock score

0, 1, or 2 possible impairment; 3, 4, or 5 suggests no impairment

Figure 4-1. The Mini-Cog™ tool is used to screen individuals at high risk for dementia.
CLOCK SCORING

A NORMAL CLOCK HAS ALL OF THE FOLLOWING ELEMENTS:
- All numbers 1–12, each only once, are present in the correct order and direction (clockwise).
- Two hands are present, one pointing to 11 and one pointing to 2.

ANY CLOCK MISSING ANY OF THESE ELEMENTS IS SCORED ABNORMAL.
REFUSAL TO DRAW A CLOCK IS SCORED ABNORMAL.

SOME EXAMPLES OF ABNORMAL CLOCKS (THERE ARE MANY OTHER KINDS)

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### SLUMS Examination

**Name: ___________________________  Age: ___________________________  Level of education: ___________________________**

<table>
<thead>
<tr>
<th>Question</th>
<th>Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. What day of the week is it?</td>
<td>__/1</td>
</tr>
<tr>
<td>2. What is the year?</td>
<td>__/1</td>
</tr>
<tr>
<td>3. What state are we in?</td>
<td>__/1</td>
</tr>
<tr>
<td>4. Please remember these five objects. I will ask you what they are later.</td>
<td>Apple, Pen, Tie, House, Car</td>
</tr>
<tr>
<td>5. You have $100 and you go to the store and buy a dozen apples for $3 and a tricycle for $20.</td>
<td>How much did you spend? __/2  How much do you have left? __/4</td>
</tr>
<tr>
<td>6. Please name as many animals as you can in one minute.</td>
<td>0-4 animals __/3  5-9 animals __/3  10-14 animals __/5  15+ animals __/2</td>
</tr>
<tr>
<td>7. What were the five objects I asked you to remember?</td>
<td>__/8</td>
</tr>
<tr>
<td>8. I am going to give you a series of numbers and I would like you to give them to me backwards. For example, if I say 42, you would say 24.</td>
<td>87 __/2  649 __/2  8537 __/2</td>
</tr>
<tr>
<td>9. This is a clock face. Please put in the hour markers and the time at ten minutes to eleven o'clock.</td>
<td>Hour markers okay __/4  Time correct __/4</td>
</tr>
<tr>
<td>10. Please place an X in the triangle.</td>
<td></td>
</tr>
</tbody>
</table>

**TOTAL SCORE**

**Questions about this assessment tool? E-mail aging@slu.edu.**

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**Figure 4-2.** Saint Louis University Mental Status (SLUMS) Examination.

visuoconstructual skills, conceptual thinking, calculations, and orientation. The MoCA examination has been found to be more effective than MMSE at differentiating patients with MCI at high risk of dementia.

Tools used in research must measure severity of disease and detect changes over time, and as such the tools are longer and take more time to administer. Clinical trials assessing cognition typically utilize the MMSE and Alzheimer's Disease Assessment Scale-cognitive subscale (ADAS-cog) for those with mild to moderate impairment and the MMSE and Severe Impairment Battery (SIB) for those with moderate to severe impairment. The Clinician’s Interview Based Impression of Change-Plus Caregiver Input (CIBIC-Plus) is a complementary assessment of cognition and function utilized in clinical trials evaluating patients with cognitive impairment. Pharmacists should be familiar with these instruments to provide adequate critique to study results.

The Alzheimer’s Disease Assessment Scale was designed to measure severity of the most important symptoms of Alzheimer disease. The ADAS-cog is considered the gold standard of cognitive tests used in clinical trials studying patients with mild to moderate cognitive impairment. Total scores range from 0 to 70, with higher scores (≥18) indicating greater cognitive impairment. A 4-point change in 6 months is recognized as a clinically important difference.

The SIB is a research tool designed to assess later stages of dementia. Overall scores can range from 0 to 100, allowing for classification of degree of impairment; lower scores indicate greater cognitive impairment. The CIBIC-Plus differs from the ADAS-cog and SIB because it relies on the caregiver interpretation of change in cognition and functioning from baseline to follow-up. The scoring ranges from 1 to 7 points, with 4 points indicating no change. A score of one point is very much improved, and a score of seven means very much worse. The CIBIC-Plus is better at estimating decline rather than improvement.

Clinical interpretation of changes in the cognitive assessments described above is controversial. In general, as patients with dementia age, their scores on the assessments will decline. Clinical trials studying the effects of medications, such as cholinesterase inhibitors or memantine, and use of some of the above measurements (e.g., MMSE, ADAS-cog, SIB) have found statistically significant improvements. However, many experts question the clinical significance of these modest improvements.

**Neuropsychiatric Assessment**

Because depression is common in the elderly, all geriatric patients presenting for the first time should be screened for depression. Screening after baseline can be done based on clinical suspicion for depression or periodically thereafter. Compared to younger adults, elderly patients with depression may not have typical signs and symptoms of depression. For this reason, the *Geriatric Depression Scale (GDS)* is a more specific screening tool for the geriatric population. The GDS is a self-report screening tool that relies on the patient to provide yes/no answers to questions about feelings and symptoms associated with depression. It has been studied and validated in multiple geriatric populations and settings including outpatient settings, nursing home settings, inpatient settings, patients with normal cognition, patients with dementia, patients with visual impairment, patients who are non-English speaking, and when administered over the telephone. The 15-item version is used when patients are fatigued or less time is available. In patients who are unwilling or unable to complete the GDS, both versions are also available in a validated informant version (GDS-I). Scoring and clinical application of the GDS is based on total points (e.g., 15 or 30), with some points awarded for positive responses and some points awarded for negative responses. A variety of scores have been used as cut-off points to indicate depre-
Geriatric Depression Scale

Choose the best answer for how you felt over the past week.

1. Are you basically satisfied with your life?            Yes/No
2. Have you dropped many of your activities and interests? Yes/No
3. Do you feel that your life is empty?                  Yes/No
4. Do you often get bored?                               Yes/No
5. Are you hopeful about the future?                     Yes/No
6. Are you bothered by thoughts you can’t get out of your head? Yes/No
7. Are you in good spirits most of the time?             Yes/No
8. Are you afraid that something bad is going to happen to you? Yes/No
9. Do you feel happy most of the time?                   Yes/No
10. Do you often feel helpless?                           Yes/No
11. Do you often get restless and fidgety?               Yes/No
12. Do you prefer to stay at home, rather than going out and doing new things? Yes/No
13. Do you frequently worry about the future?            Yes/No
14. Do you feel you have more problems with memory than most? Yes/No
15. Do you think it is wonderful to be alive now?         Yes/No
16. Do you often feel downhearted and blue?              Yes/No
17. Do you feel pretty worthless the way you are now?    Yes/No
18. Do you worry a lot about the past?                   Yes/No
19. Do you find life very exciting?                      Yes/No
20. Is it hard for you to get started on new projects?    Yes/No
21. Do you feel full of energy?                          Yes/No
22. Do you feel that your situation is hopeless?          Yes/No
23. Do you think that most people are better off than you are? Yes/No
24. Do you frequently get upset over little things?      Yes/No
25. Do you frequently feel like crying?                  Yes/No
26. Do you have trouble concentrating?                   Yes/No
27. Do you enjoy getting up in the morning?              Yes/No
28. Do you prefer to avoid social gatherings?            Yes/No
29. Is it easy for you to make decisions?                Yes/No
30. Is your mind as clear as it used to be?              Yes/No

Figure 4-3. Geriatric Depression Scale.

sion; in general, the higher the score the more severe the depression.

In addition to the GDS, clinicians may prefer to use quicker tools to screen for depression, such as the Patient Health Questionnaire (PHQ)-2 and PHQ-9 assessments. With two and nine questions, respectively, these tools are applicable to a broad range of patients. Patients testing positive for depression with the PHQ-2 should be further assessed by the PHQ-9. Although there have been multiple studies using these tools to screen for depression in older adults, some symptoms included in the PHQ-9 questions (e.g., trouble with sleep, moving or speaking slowly, and feeling tired or having little energy) are nonspecific and may be responded to positively in many older adults without depression. Nevertheless, the PHQ-9 has been found to screen for depression equally as well as the GDS-15 in ambulatory older adults.46

**KEY POINT:** The GDS is a more specific screening tool for the geriatric population than other depression screening tools.

If a patient has dementia and needs to be assessed for depression, the GDS or GDS-I can be used. In addition, the Dementia Mood Assessment Scale and the Cornell Scale for Depression in Dementia are screening tools that were developed specifically for this population. Both scales are completed by a caregiver or nursing staff. Because of poor specificity in patients with cognitive impairment, the PHQ-2 and PHQ-9 may not be the most appropriate choices to screen for depression in this patient group.47

In patients with dementia, psychotic and behavioral problems can also occur as the disease state progresses. Assessment of psychotic and behavioral problems in patients with dementia and the ability of the caregiver(s) to cope with the problems is important to evaluate the safety of the patient and the ability to stay in the same living situation. Several rating scales are available for behavioral assessment.

The Neuropsychiatric Inventory (NPI), Behave-AD (Behavioral Pathology in Alzheimer’s Disease Rating Scale), and NPI-Q (Neuropsychiatric Inventory Questionnaire) are commonly used assessments of behavioral problems.48-50 The NPI, Behave-AD, and CIBIC-Plus are longer assessments used mainly in research settings and clinical trials, whereas the NPI-Q was developed for clinical practice. The CIBIC-Plus, an assessment tool described above (see Cognitive Assessment), includes components of behavioral assessment and is also used to evaluate these symptoms in clinical trials.

The NPI is a validated evaluation of neuropsychiatric symptoms based on a structured interview conducted by a provider with a caregiver and takes about 10 minutes to complete. It includes 12 symptom domains rated for frequency and severity by the caregiver, for a total of 144 points. Higher scores indicate more severe neuropsychiatric illness. This tool has been translated into multiple languages, and clinical trials, both in and outside the United States, often use the NPI as a secondary outcome for drugs being studied for dementia. The NPI-NH (developed for use in nursing homes) can be completed by certified nurses’ aides and licensed vocational nurses for use as a tracking agent for behavioral changes.51 The Behave-AD is one of the earliest neuropsychiatric rating scales similar to the NPI; it is often included in clinical trials of drug treatments in patients with Alzheimer disease. The Behave-AD is a validated tool that evaluates 25 neuropsychiatric symptoms in seven categories and includes a global rating of caregiver stress associated with the symptoms. The Behave-AD takes approximately 20 minutes to administer.

The NPI-Q is a validated questionnaire for clinical practice that can typically be completed in 5 minutes or less. It has the same symptom domains as the NPI: the caregiver-informant rates the severity of behavioral symptoms and the distress on the caregiver. Scores on the NPI-Q range from 0 to 60, with higher numbers indicating increased severity of symptoms and increased stress on the caregiver. The NPI-Q has been translated into Spanish.
Similar to the cognitive tests described previously, the definition of clinically significant changes in neuropsychiatric tests is debatable. Clinical trials studying drugs for Alzheimer disease typically find statistically significant changes in these assessments, but it is very difficult to tell if these changes are clinically relevant as a whole. It may be useful to refer complex patients to a neurologist or neuropsychologist for further evaluation and recommendation. Although pharmacists are likely to interact and recommend treatment for patients with neuropsychiatric symptoms, it is unlikely that they will be involved with neuropsychiatric screening beyond use of the GDS screening tool for depression.

**Functional Assessment**

Functional assessments of geriatric patients should be performed at the initial visit and at regular intervals (e.g., annually) to assess for changes in function that might require changes in living situation. A comprehensive functional assessment should include assessing activities of daily living (ADLs), instrumental activities of daily living (IADLs), gait and balance, fall risk, and current level of physical activity. Geriatric nurses, social workers, occupational therapists, physical therapists, and caregivers are especially helpful in performing functional assessments of patients. Specifically, occupational therapists are typically trained in assessing and making recommendations to improve ADLs and IADLs. Physical therapists are helpful for assessing and intervening on gait and balance problems, fall risk, level of physical activity, and use of assistive devices for walking. Multiple tools are available to assist with assessing function. Utilizing these tools in clinical practice may help detect impairments that may not be adequately recognized by clinicians.52

Basic ADLs include self-care activities that are required to sustain existence and independence, such as bathing, dressing, toileting, transferring from bed or chair, continence, feeding, grooming, and walking. Patients should be evaluated to determine whether they are capable of performing ADLs independently, with help, or if they are dependent on others to perform them. Based on patients' ability to perform ADLs independently, they might require assistance that varies from needing to have a caregiver check on them several times a week, living with a caregiver or in an assisted living facility, or living in a long-term care center (e.g., nursing home). Physicians can also order home healthcare, including nursing, physical therapy, and occupational therapy, for patients who need assistance at home. Home healthcare agencies paid by Medicare are required to perform a formal assessment of a patient's need for care (Outcome and Assessment Information Set [OASIS]), including the ability of the patient to perform ADLs and IADLs.53 These data are utilized by Medicare to monitor the quality of home healthcare but can also be used by healthcare practitioners to monitor patient-specific quality of care.

Multiple tools are available to assist in documenting ADL assessments. The Katz ADL tool is one of the oldest tools used in clinical practice and takes about 5 minutes to administer.54 The tool scores patients 1 point for being independent with six categories of ADLs (bathing, dressing, toileting, transferring, continence, and feeding) and 0 points for dependence with the activities. Higher points indicate more independence and functioning. The Alzheimer's Disease Cooperative Study Activities of Daily Living Inventory (ADCS-ADL) tool is more detailed; typically used in research settings and clinical trials, it includes an assessment of ADLs and IADLs. The ADCS-ADL is a caregiver-rated questionnaire assessing 23 items; higher scores indicate better functioning.55 This tool is capable of assessing function in a wider range of patients with cognitive impairment than the Katz ADL tool. Both tools can be used with patients living in a variety of care settings and those of different cultural and ethnic backgrounds.

IADLs consist of more complex activities that are necessary to have a higher level of func-
tioning. The Lawton IADL tool is commonly used in clinical practice and takes about 10 minutes to administer. It assesses the ability to complete the following eight tasks: ability to use a telephone, shop, prepare meals, maintain light housework, do laundry, travel independently, take medications, and handle finances. Some IADLs are learned skills and may be more a function of a patient's environment and previous training than ADLs. A higher score on the Lawton IADL also indicates higher functioning. IADL tools can be completed by either the patient or a caregiver and can be utilized in culturally diverse settings.

The Functional Assessment Screening (FAST) scale is an additional tool often used in clinical trials evaluating patients with dementia, or by palliative care, hospice, and dementia healthcare teams to evaluate and/or monitor the ability of a patient to perform basic ADLs. The FAST scale is divided into seven major stages, from normal (FAST stage 1) to severe dementia (FAST stage 7). Stages 6 and 7 are further divided into substages indicating loss of specific types of independence (e.g., ability to dress independently) or abilities (e.g., ambulation).

**Falls, Gait, Balance, and Physical Activity**

A patient's recent fall history (e.g., last 1–3 months) should be assessed at all medical visits, and future fall risk should be assessed regularly (e.g., annually). Assessing fall risk requires the assessment of many factors, such as drugs (e.g., sedative/hypnotics) and disease states (e.g., heart disease, osteoarthritis, Parkinson disease) in addition to gait, balance and strength, and home safety (e.g., rugs, loose floor boards, stairs, cluttered areas).

Both gait and balance can be assessed utilizing the Berg Balance Scale (BBS) and the Timed Up and Go Test (TUG). The BBS requires individuals to complete 14 balance-challenging tasks of varying difficulty without any assistive devices. For instance, the patient is asked to go from a sitting position to a standing position, to transfer between two chairs, to pick up an object from the floor, to stand in tandem stance, and to stand on one leg. Each item is scored on a 5-point scale, with higher ratings indicating better performance. The highest number of points that patients can achieve is 56, with 45 points and higher typically used as the cut-off for patients who are not likely to fall. This scale has good specificity (96%) for detecting non-fallers. It takes approximately 10–15 minutes to administer and requires some equipment (e.g., chairs, stopwatch, yardstick, line on floor).

The TUG is easier and quicker than the BBS in assessing fall risk. The patient must sit in a chair, safely rise from the chair, walk around a visibly colored marker (e.g., orange cone) three meters away, walk back, and then sit down in the chair. Patients must be instructed to do all of this as quickly and safely as they can. They can use their assistive devices while taking the test, but this typically slows them down. The test is timed; those who complete the test in less than 20 seconds have been shown to be independent in their transfers and mobility, and those requiring 30 seconds or longer have higher dependence and frailty. In another study of the TUG, investigators found that older adults who take longer than 14 seconds to complete the test are at a high fall risk. Patients completing the test more quickly can still be counseled to consider balance exercises, and those in the high-risk group should be advised to seek further assessment and intervention for falls.

Assessment of physical activity is also important in the ambulatory elderly, as increased physical activity has been shown to be an important predictor of functional status. Surgeon General and American Heart Association (AHA) guidelines suggest 30 minutes or more of moderate physical activity on five or more days of the week. The AHA guidelines also provide very detailed recommendations for strengthening and stability. Older sedentary adults can improve physical functioning by meeting these suggested physical activity levels; dropping below these levels has a negative effect on function. Patients should be interviewed about the
type of physical activity that they are involved in and the amount of time they are spending doing particular activities. Relatively brief counseling about walking and strength exercise has been shown to increase physical activity in elderly patients. Patients may be motivated to engage in physical activity because it has been shown to reduce mortality and maintain functioning in older adults compared with a sedentary lifestyle, even if the physical activity is initiated at an advanced age.

Social Assessment

Social assessment of the elderly includes some traditional aspects of a medical assessment of a younger patient (e.g., smoking, alcohol status) but moves beyond that to include areas essential to caring for an older adult (e.g., independence, advance directives, insurance status, transportation/driving status, sexual activity, life changes). Social workers can provide invaluable assistance and information for clinicians, patients, and caregivers when performing a complete social assessment. Social assessments may need to be tailored to the patient's cultural and religious preferences.

KEY POINT: Social assessment includes areas essential to caring for an older adult: independence, advance directives, insurance status, transportation/driving status, sexual activity, and life changes.

Recent life changes should be considered to fully appreciate goals that elderly patients may have for their healthcare. Many elderly will have faced new life changes, such as the death of a spouse, illness, moving from their home to an assisted living situation, and/or dealing with the reality of their own eventual death. It is important to understand how patients deal with these changes and how they perceive themselves in order to determine their overall adaptability to life changes.

Social History: Tobacco and Alcohol Use

Although most people do not start smoking in advanced age, it is important to determine the current smoking status of older adults, as those who do smoke probably have a significant smoking history. Similar to younger adults, patients should be asked about the length of their smoking history, how many cigarettes per day they smoke, and about attempts to quit. In addition, it is important to assess a patient's willingness to quit. Many elderly may believe that they will not see a benefit from smoking cessation at this point in their lives. However, there is evidence to show that smoking cessation at any age, even after age 65, is beneficial for reducing overall risk of death and disability. If a patient is willing to quit smoking, assistance with a plan, whether pharmacologic or nonpharmacologic, should be offered.

In addition to tobacco use, information about alcohol consumption should be elicited from elderly patients. Occasional alcohol use may be permitted if it increases quality of life, but heavy or persistent alcohol use can cause complications in the elderly. For example, alcohol may increase a patient’s risk for falls and fractures by impairing judgment and increasing balance problems. Also, chronic alcohol consumption may result in impaired hepatic function, altering metabolism of medications. Because many elderly are on multiple medications, there is a high likelihood they will be on at least one medication that is hepatically metabolized. Furthermore, it is important to assess alcohol consumption in elderly patients who become hospitalized in order to prevent delirium tremens, a potentially life-threatening consequence of alcohol withdrawal. Older adults are likely to have a higher blood alcohol level than younger people for a given dose of alcohol due to their less efficient hepatic metabolism. If proper assessment of alcohol use is not performed, there is an increased risk of developing delirium tremens when chronic drinkers are admitted to the hospital.
Independence

Independence should be evaluated as described above in the functional assessment. If the patient lives in an assisted living facility, the contact information for the facility should be recorded. A complete list of healthcare providers (e.g., specialists) should be recorded for future reference. Family and caregiver information should also be recorded at the initial visit and updated as needed. If an elderly patient has multiple family contacts, it is important to have a primary contact designated so healthcare providers are aware of which person to contact first. It is helpful to have this information available before a patient becomes severely ill. If the patient utilizes medication administration assistance, this information should also be recorded in case medication orders need to be submitted to a facility in addition to the pharmacy.

In some cases, tests of cognitive impairment or functional assessment do not clearly identify problems with the executive function required to manage medications or adhere to a treatment plan. Tests focused on executive dysfunction, such as the EXIT-25 or the Frontal Assessment Battery, can be administered to objectively identify functional problems that may limit a patient’s ability to live alone or manage his or her medications, indicating a need for assistance or a change in living situation to ensure patient safety.

Advance Directives

Assessment of advance directives (ADs) is a vital, but sometimes neglected, part of the medical assessment of elderly patients. ADs are legal documents that allow patients to have their medical decisions known and followed when receiving care. These are so important to assess that in 1990 the Federal Patient Self-Determination Act was passed, requiring that patients be asked at the time of admission to a healthcare service whether they have advance care plans. ADs must be documented when patients still have the capacity to make healthcare decisions. Once an initial assessment of ADs is made, it is important to regularly reassess a patient’s wishes because they can change as the patient ages or develops new health problems. Advance care plans can be revised up until the last moment of capacity to make decisions, so it is also important for healthcare providers to assess whether the most current decisions are on record.

Establishing whether ADs exist is important not only for a patient but also for the family. Having ADs in place alleviates some stress and anxiety for family members. In many situations, cultural and religious preferences may impact the ADs of the patient and should always be considered in discussions. Further information regarding ADs is included in Chapter 2.

Insurance Coverage

Another important assessment topic is insurance coverage, both government-provided (Medicare, Medicaid, and military service) and private. Most elderly will have Medicare coverage, and many will supplement coverage with an additional privately secured insurance plan. It is important to determine a person’s eligibility for Medicare, because the coverage is associated with significant improvements in self-reported health trends for previously uninsured patients, especially for cardiovascular disease or diabetes. Patients can enroll in Medicare Part A, B, and/or D. Medicare Part A covers hospitalizations; Part B covers outpatient medical visits, infusions, most immunizations, and medical supplies; and Part D covers prescriptions and MTM. However, Medicare coverage is not free of charge other than for Medicare Part A. Patients must pay for Medicare Part B and D coverage and plan deductibles and copays for products and services, unless they have supplemental coverage for these expenses. Medicare Part D covers prescription drugs for any person with Medicare Part B. Some elderly may qualify for extra help, depending on their income in comparison to the federal poverty levels. These dollar amounts fluctuate, so checking the Medicare and Social Security websites is important to determine whether a patient may qualify for extra help. If the patient qualifies, then his or her Medicare copays may be reduced or eliminated.
For patients with Medicare Part D it is also advantageous to assess when and if they will be in the “doughnut-hole” coverage gap. Depending on the plan, during this time the patient may be responsible for all prescription drug costs until he or she spends up to a particular dollar amount designated by the selected Medicare Part D plan. Elderly patients with no prescription benefits while in this coverage gap may become nonadherent with their medications because of cost. These coverage gaps are to be eliminated in the future.

Transportation and Driving Assessment

Understanding transportation and driving ability in the elderly is extremely important, as geriatrics may not be able to come to appointments regularly, pick up their medications, shop for groceries, or have social outlets. Assessing an elderly person’s ability to drive is important in balancing the individual’s independence with personal (and public) safety. This assessment is particularly important for people with cognitive impairment or perception deficits such as decreased vision, arthritis, seizures, stroke, diabetes, or Alzheimer disease. Many elderly link driving with independence and rely on it for daily activities. Due to this, it may be difficult to convince them they are no longer safe to operate a motor vehicle. Social support from family and friends is essential for elderly patients to arrive at a decision to stop driving. Because many states do not require drivers to come into the Department of Motor Vehicles each time they renew their licenses, caregivers, family members, clinicians, and even patients must play an important role in assessing driving ability. When a patient has been shown to be an unsafe driver, a referral should be made to the proper organization per each state’s protocol; if a patient is no longer able to independently operate a motor vehicle, it becomes important to assess his or her ability to use other modes of transportation.

The ability to use other modes of transportation should be assessed for patients who do not drive. Depending on the living situation of the individual, transportation may be included with his or her housing. If not, those living in more rural areas may not have access to public transportation, whereas those in urban areas may have safety concerns with public transportation. In urban areas, nonprofit programs such as Access-A-Ride can provide low-cost transportation for elderly patients with functional deficits. An assessment completed by a physician may be required to determine eligibility. Depending on the state, Medicaid may also provide some payment for transportation, including taxi fares. Pharmacists can help patients with transportation challenges by reviewing local options for low-cost transportation and by referring patients to social workers who may have additional transportation resources.

Sexual Activity

An assessment of sexual activity may be overlooked in the elderly due to a perception that they are not sexually active. The sexual activity of elders is often underestimated, and monogamy should not be assumed. Elders are still at risk for acquiring sexually transmitted diseases when sexually active with multiple partners or a single new untested partner. Although adults over age 55 make up the smallest group of HIV positive individuals in the United States, this age group is growing as treatments prolong life expectancy. If an elderly person is active and not practicing safe sex, he or she should also be screened for and educated about sexually transmitted diseases.

On the other hand, many elderly suffer from sexual difficulties such as impotence, decreased libido, atrophic vaginitis, and dyspareunia. Therefore, patients should also be questioned about their desire to remedy these problems and improve their sexual experience. In many instances, these problems may be improved with medication or vaginal lubricants. Unfortunately, the biggest barrier to these improvements is often communication between the provider and patient.
Case 1: Comprehensive Interprofessional Geriatric Assessment

Setting:
- Ambulatory.

Subjective:
MP is an 85-year-old woman who is new to the community. She recently moved to an assisted living facility in your area, as she was recently widowed. Previously, she lived with her husband in their own home. Her daughter requested she move into the assisted living facility, as it is close to her daughter’s home. She relies on the facility to provide assistance for cooking, cleaning, and medication management. She is initiating care at a local seniors clinic for the first time. Your consulting firm provides clinical pharmacist services at the assisted living facility and at the seniors clinic where she is scheduled for a new patient appointment. Her daughter asks what to expect at the first visit.

Past Medical History:
- Mild cognitive impairment, osteoporosis, hypertension, osteoarthritis, insomnia, and anemia.

Medications:
- Acetaminophen, aspirin, alendronate, lisinopril, hydrochlorothiazide, zolpidem, ranitidine as needed, multivitamin, and calcium/vitamin D.

Social History:
- No history of smoking; occasional alcohol socially.

Family History:
- Sister died of a stroke 3 years ago, otherwise unknown.

Assessment:
MP will undergo comprehensive geriatric assessment at the seniors clinic, and she and her daughter want to know what to expect.

Plan:
Provide education to patient and caregiver on items involved in comprehensive geriatric assessment by an interprofessional team. Reassure that these assessments may take more than one visit.

1. Medical history: past medical records, immunization history (pneumococcal, influenza, herpes zoster, tetanus), history of falls and fall risk, gait and balance, physical activity and current diet, history of osteoporosis (past DEXA results).
2. Social history and functional status: ADs, assisted living contact information, transportation, driving ability, sexual activity, recent life changes, ADLs, IADLs, insurance status.
4. Physical assessment: vital signs (including pain score), height and weight, hearing and eye tests, physical examinations, oral examination.
5. Laboratory: thyroid, vitamin B12, complete blood count, basic metabolic panel, fasting lipid panel, vitamin D.
6. Neuropsychiatric assessment: screening for depression (GDS or GDS-I), cognitive impairment (SLUMS, 7MS, or MoCA), and possibly other neuropsychiatric screening depending on results.
7. Medication review: review of her medications (including OTC agents) for drug therapy problems.

Rationale:

1. A comprehensive interprofessional geriatric assessment does not always occur in routine medical practice. Problems both simple and complex can be missed in assessment of the elderly patient due to atypical disease presentation and an attitude that many symptoms are normal in the aging adult. Establishing care at an interprofessional senior clinic will provide MP the best opportunity to attain optimal health and well-being.

2. The medical history will establish the baseline of disease states present and preventive services necessary for MP. Social and functional history will allow appropriate referrals for social services and support. They will also assist with gauging the need for services to be provided by her assisted living facility, as these services can be very expensive. The review of systems and physical assessment will identify what additional tests and evaluations may be needed and will discover if disease targets are being met (e.g., hypertension). Laboratory tests will evaluate MP’s anemia, fracture risk, and whether there are reversible causes of cognitive impairment, such as hypothyroidism, low hemoglobin, or low vitamin B12. Neuropsychiatric testing will establish the severity of the cognitive impairment and possibly clarify symptoms of insomnia. Other causes of these problems, such as depression, may be established. Finally, a medication review will enable the assisted living facility and caregiver to know what medication management issues may be present. Establishing the pattern of use for prescription and OTC medication in this patient may uncover reversible causes of cognitive impairment (e.g., zolpidem) and insomnia. Certain medications might be discontinued (e.g., aspirin, alendronate, multivitamin) if not clearly indicated.
Case 2: Reassessment by a Consultant Pharmacist in the Long-Term Care Setting

Setting:
Long-term care.

Subjective:
MP is now 88 years old and is entering a long-term care setting because of advancing dementia with hallucinations and delusions. The consultant pharmacist who serves the long-term care facility must identify needed evaluations for assessment of MP’s medication regimen.

Past Medical History:
Alzheimer disease, osteoporosis, hypertension, osteoarthritis, depression, hypothyroidism, constipation, hallucinations, delusions.

Medications:
Acetaminophen, low-dose aspirin, ibandronate, lisinopril, levothyroxine, risperidone, rivastigmine, zolpidem, multivitamin, calcium/vitamin D, hydrocodone/acetaminophen as needed, esomeprazole as needed, and milk of magnesia as needed.

Social History:
No history of smoking; no alcohol.

Family History:
Sister died of a stroke 6 years ago, otherwise unknown.

Assessment:
Additional information required for initial pharmacist consultation.

Plan:
Obtain the following information/tests:
Information from MP, her daughter, or the nursing staff regarding sleep habits, bowel habits, ADLs, and insurance status (including formulary listings). Physical assessments should include her current vital signs, pain assessment using a pain rating scale that she can respond to, height, and weight. Laboratory measurements for TSH, basic metabolic panel, and CBC are requested. Neuropsychiatric evaluations to review include MMSE, NPI-NH, and GDS-I. Frequency of administration of acetaminophen, risperidone, zolpidem, hydrocodone/acetaminophen, esomeprazole, and milk of magnesia should be obtained from the medication administration record.

Rationale:
1. Both subjective and objective information will aid in evaluation of the effectiveness and risk-benefit ratio of several of MP’s medications. The continued need for risperidone, rivastigmine, and zolpidem require special scrutiny of the objective neuropsychiatric assessments, as well as physical examination, laboratory findings, and pain ratings. Inadequately treated pain, constipation, or hypothyroidism in MP could manifest themselves as agitation resulting in inappropriate use of psychotropic medications. New conditions, such as hyponatremia or a urinary tract infection, could also cloud the picture.

2. Whether MP has Medicare Part D or other insurance to cover prescription medications should be determined. Admission to a nursing home involves a different Medicare Part D insurer that includes a long-term care pharmacy provider, which may be advantageous to MP. Her medications should be reviewed to identify potential opportunity to convert to generic or preferred brand name prescriptions to reduce costs without reducing quality of care.


**Clinical Pearls**

- Atypical disease presentation is often seen in frail, elderly patients. In a patient with dementia, delirium may be the presenting symptom for many illnesses including a urinary tract infection, a myocardial infarction, or anemia. The organ system that is weakest in an individual patient is frequently the first to exhibit symptoms. Basic laboratory assessments (e.g., CBC, comprehensive metabolic panel, and urinalysis) may help direct further work-up and treatment.

- Pharmacists documenting assessments as part of MTM services can alert the provider if specific assessments need further follow-up or monitoring. The pharmacist may be the first healthcare provider to become aware of social, functional, or cognitive deficits when a patient has problems managing medications.

**Chapter Summary**

A comprehensive assessment of geriatric patients encompasses multiple types of assessments including medical, cognitive, neuropsychiatric, functional, and social assessments. Elderly patients presenting to a primary care provider for the first time should attempt to bring previous medical records. If possible, family and caregivers should also accompany them to the visits to provide supporting information. Completing all of the necessary assessments may take several visits with a primary care provider.

**Self-Assessment Questions**

1. How might the physical examination be different for ambulatory elderly compared to more frail, institutionalized elderly patients?

2. When screening for common conditions in the elderly, what laboratory parameters are commonly evaluated?

3. How is cancer screening in the geriatric patient different when the patient becomes older and frailer?

4. What specific areas should a pharmacist focus on when performing a medication assessment?

5. What are the major differences between the tools commonly used for cognitive assessment?

6. How might a clinician implement a tool into his or her clinical practice to evaluate geriatric patients for neuropsychiatric problems?

7. What are the tools available to help assess functional abilities, and how can they be specifically utilized?

8. What are the important aspects of a complete social assessment for elderly patients?

9. Which interprofessional team members help contribute to a comprehensive assessment of a geriatric patient?

**References**


34. Dong Y, Lee WY, Basri NA, et al. The Montreal Cognitive Assessment is superior to the Mini-Mental State Examination in detecting patients at higher risk of dementia. *Int Psychogeriatr.* 2012;24:1749–1755.


Learning Objectives

1. Define the term *suboptimal drug use* and discuss the prevalence of the three different types in the elderly.
2. Define the term *adverse drug event* and discuss the epidemiology of the three different types in the elderly.
3. Describe evidence-based data from randomized controlled trials designed to improve suboptimal drug use and reduce adverse drug events for geriatric patients in different settings.
4. Describe medication therapy management techniques used to improve suboptimal drug use in the elderly.

Key Terms and Definitions

**ADVERSE DRUG EVENT:** Undesirable health outcome associated with drug therapy due to an adverse drug reaction, an adverse drug withdrawal event, or therapeutic failure.

**ADVERSE DRUG REACTION:** An appreciably harmful or unpleasant reaction resulting from an intervention related to the use of a medicinal product, which predicts hazard from future administration and warrants prevention or specific treatment, alteration of the dosage regimen, or withdrawal of the product.

**ADVERSE DRUG WITHDRAWAL EVENT:** A clinical set of symptoms or signs that are related to the removal of a drug.

**INAPPROPRIATE MEDICATION:** Use of a medication whose potential risks outweigh its potential benefits or that does not agree with accepted medical standards.

**THERAPEUTIC FAILURE:** Adverse health event due to failure to accomplish the goals of treatment resulting from inadequate or inappropriate drug therapy and not related to the natural progression of disease.
**UNDERUSE OF MEDICATION:** Omission of or too low a dose of a needed drug for an established active disease or condition.

**UNNECESSARY MEDICATION:** Medication that is prescribed or used without a supporting indication, lacks effectiveness, or is a therapeutic duplication of another medication or drug.

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**Introduction**

Medications may be prescribed to prevent the onset of disease, treat symptoms or complications of chronic illness, or cure diseases. Older adults also frequently self-medicate with over-the-counter (OTC) medications and dietary supplements. Indeed, over one-third of community-dwelling older adults aged 75 and older take five or more prescription medications, and over half take OTC or dietary supplements that are frequently not reported to health professionals unless specifically queried. In U.S. nursing homes, 40% of older residents take nine or more medications. Although these medications may be beneficial, drug-related problems may also occur. Specifically, medications can be suboptimal (i.e., too much, too little, or the wrong drug) and adverse drug events (ADEs) (undesirable health outcomes associated with drug therapy) may occur.

This chapter will elaborate how common types of suboptimal drug use due to potentially unnecessary medications, inappropriate medications, and/or underuse of medications occur in older adults. ADEs will also be highlighted by reporting how often adverse drug reactions, adverse drug withdrawal events, and therapeutic failure occur in older adults. Moreover, information will be discussed about findings from randomized controlled trials designed to improve suboptimal drug use and reduce ADEs. Finally, the chapter will end with a discussion about the role of pharmacists in conducting medication therapy management to reduce these drug-related problems.

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**Suboptimal Drug Use**

**Unnecessary Medications**

Few studies have quantified the prevalence of unnecessary medication use. A study of unnecessary drug use in a frail elderly Veterans’ Affairs (VA) population defined unnecessary drug use as a drug that lacks an indication, effectiveness, or is a therapeutic duplication. They found that 44% of veterans had at least one unnecessary medication at hospital discharge. The reasons for an unnecessary medication included lack of indication (33%), lack of efficacy (19%), and therapeutic duplication (8%). The most common unnecessary medications included gastrointestinal agents, central nervous system agents, and nutrients and minerals. Another study in an outpatient VA population reported that approximately 60% of the patients had a medication that was ineffective, not indicated, or was a duplication of another drug. It was also noted that as the numbers of medications a patient was taking increased so did the average number of unnecessary drugs. Evaluation of unnecessary drug use in another outpatient VA population also found that approximately 60% had at least one unnecessary medication. The most common reason for unnecessary drug use was lack of efficacy. Interventions to reduce unnecessary drug use include incorporating a pharmacist into an interprofessional team, pharmacist-led medication reviews, academic detailing, feedback reporting, and physician medication review.
Inappropriate Medications

The second form of suboptimal drug use is inappropriate medication. In 1991, a set of explicit criteria were developed via Delphi survey of U.S. geriatric experts that is commonly referred to as the Beers criteria. These explicit criteria have subsequently been updated three times; the most recent is an evidence-based approach supported by the American Geriatrics Society for drugs to avoid (also commonly referred to as high-risk drugs) and drug–disease interactions. Various U.S. and non-U.S. groups have adopted some specific criteria for use as quality indicator measures in various populations of elders. Table 5-1 shows a list of high-risk drugs planned to be used as quality indicators by the National Committee for Quality Assurance (NCQA) based in part on the Beers criteria. Notable additions to the high-risk drug list include glyburide and megestrol, two medications not previously included in earlier iterations of these criteria. Glyburide has been shown to have an increased risk of severe and prolonged hypoglycemia, whereas megestrol has been shown to have an increased risk of thrombotic events. Previous studies evaluating prescribing patterns of potentially inappropriate medications (not including these new additions) showed that between 12.3% and 21.5% of older outpatients received one or more high-risk medications. Drugs that can potentially exacerbate three common diseases in older adults (i.e., dementia, history of falls or fractures, and chronic kidney disease) were also selected by NCQA as quality measures. Table 5-2 shows the drug–disease interactions proposed for 2014, with the only notable addition being anticonvulsants in those with a history of falls or fractures. Previous studies using these criteria (excluding the anticonvulsant/falls or fracture interaction) reported that the prevalence of drug–disease interactions was 15.2% to 19.4% in older outpatients; the most common problem was the use of highly anticholinergic medications in those with dementia.

| Table 5-1. High-Risk Medications in the Elderly per NCQA HEDIS Criteria |
|--------------------------------|---------------------------------|
| **Therapeutic Class** | **High-Risk Medication(s)** |
| Anticholinergics, 1st generation antihistamines | Brompheniramine, Carbinoxamine, Chlorpheniramine, Clemastine, Cyproheptadine, Dextromethorphan, Dextropropoxyphene, Diphenhydramine (oral), Doxylamine, Hydroxyzine, Promethazine, Triprolidine |
| Anticholinergics, for Parkinson disease | Benztropine (oral), Trihexyphenidyl |
| Anti-infectives, other | Nitrofurantoin, Nitrofurantoin macrocrystals, Nitrofurantoin monohydrate/macrocrystals |
| Antiplatelets | Dipyridamole, oral short-acting Ticlopidine |
| Cardiovascular, alpha agonists, central | Guanabenz, Guanfacine, Methyldopa, Reserpine >0.1 mg/day |
| Cardiovascular, other | Disopyramide, Digoxin >0.125 mg/day, Nifedipine, immediate release |
| Central nervous system, tertiary tricyclic antidepressants | Amitriptyline, Clomipramine, Imipramine, Trimipramine |
| Central nervous system, barbiturates | Amobarbital, Butobarbital, Butalbital, Mephobarbital, Pentobarbital, Phenobarbital, Secobarbital |
| Central nervous system, vasodilators | Ergot mesylates, Isoxsuprine |
| Central nervous system, other | Chloral hydrate |
In Europe, the development and use of complementary explicit criteria, called STOPP (Screening Tool of Older Person’s Prescriptions), not only considers drugs to avoid and drug–disease interactions but other important aspects of optimal prescribing, including therapeutic duplication, duration of use, dosage, and drug–drug interactions. In addition, there are explicit criteria for excessive drug dosage, such as for drugs that are primarily cleared renally. Any of these criteria can be helpful in the review of an individual patient’s drug regimen, but they can also be employed to evaluate prescribing patterns among populations of patients. For this, criteria can be applied to data sets such as pharmacy claims data or managed care data. Although these explicit criteria are easily applied to computerized pharmacy claims data, this evaluation is controversial, because the criteria are out of date as soon as they are published. Moreover, it is difficult to consider patient-specific characteristics that may make a potentially inappropriate medication appropriate for a specific patient.

### Table 5-1. (cont’d)

<table>
<thead>
<tr>
<th>Therapeutic Class</th>
<th>High-Risk Medication(s)</th>
</tr>
</thead>
</table>
| Central nervous system, other | Thoridazine  
Meprobamate |
| Central nervous system, nonbenzodiazepine hypnotics | Eszopiclone  
Zaleplon  
Zolpidem |
| Endocrine system, estrogens with or without progestins | Conjugated estrogen  
Esterified estrogen  
Estradiol  
Estropipate |
| Endocrine system, sulfonylureas, long duration | Chlorpropamide  
Glyburide |
| Endocrine system, other | Megestrol  
Desiccated thyroid |
| Gastrointestinal system, other | Trimethobenzamide |
| Pain medications, skeletal muscle relaxants | Carisoprodol  
Chlorzoxazone  
Cyclobenzaprine  
Metaxalone  
Methocarbamol  
Orphenadrine |
| Pain medications, specific nonsteroidal anti-inflammatory drugs | Indomethacin  
Ketorolac, oral and parenteral |
| Pain medications, specific opioids | Meperidine  
Pentazocine |

**HEDIS, Healthcare Effectiveness Data and Information Set**

See reference 13 for more information.

### Table 5-2. Potentially Harmful Drug–Disease Interactions in the Elderly per NCQA HEDIS Criteria

<table>
<thead>
<tr>
<th>Disease</th>
<th>Potentially Harmful Drug(s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Falls</td>
<td>Anticonvulsants</td>
</tr>
<tr>
<td></td>
<td>Benzodiazepines</td>
</tr>
<tr>
<td></td>
<td>Nonbenzodiazepine hypnotics (i.e., barbiturates, chloral hydrate, “Z” drugs [eszopiclone, zaleplon, zolpidem])</td>
</tr>
<tr>
<td></td>
<td>Tricyclic antidepressants (both tertiary and secondary)</td>
</tr>
<tr>
<td></td>
<td>SSRIs</td>
</tr>
<tr>
<td></td>
<td>Antipsychotics</td>
</tr>
<tr>
<td>Dementia</td>
<td>Tricyclic antidepressants (both tertiary and secondary)</td>
</tr>
<tr>
<td></td>
<td>Antipsychotics</td>
</tr>
<tr>
<td></td>
<td>H₂ blockers</td>
</tr>
<tr>
<td></td>
<td>Anticholinergics</td>
</tr>
<tr>
<td></td>
<td>Benzodiazepines</td>
</tr>
<tr>
<td></td>
<td>Nonbenzodiazepine hypnotics (i.e., barbiturates, chloral hydrate, “Z” drugs [eszopiclone, zaleplon, zolpidem])</td>
</tr>
<tr>
<td>Chronic kidney disease/chronic renal failure (eGFR &lt;30 mL/min)</td>
<td>All NSAIDs</td>
</tr>
</tbody>
</table>

NSAIDs, nonsteroidal anti-inflammatory drugs; SSRIs, selective serotonin reuptake inhibitors. See reference 16 for more information.
Another approach to determining inappropriate drug use is the use of implicit criteria such as the Medication Appropriateness Index (MAI) (Table 5-3).10,19 The MAI consists of 10 questions and has extensive instructions for use and good-to-excellent reliability and predictive validity.10 When the MAI is applied to the drug regimens of older adults being discharged home from the hospital, up to 92% had some potential inappropriate prescribing problems, commonly in the domains of dosage, directions, and medication cost.20 Some potential advantages to using the MAI is that it allows for consideration of patient-specific characteristics found in a medical record, is very sensitive in detecting potential problems, and is never out of date. Disadvantages of the MAI are the time required (up to 10 minutes per drug) and the high level of drug therapy expertise required of evaluators.

Table 5-3. Medication Appropriateness Index

<table>
<thead>
<tr>
<th>Questions to ask about each individual medication:</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Is there an indication for the medication?</td>
</tr>
<tr>
<td>2. Is the medication effective for the condition?</td>
</tr>
<tr>
<td>3. Is the dosage correct?</td>
</tr>
<tr>
<td>4. Are the directions correct?</td>
</tr>
<tr>
<td>5. Are the directions practical?</td>
</tr>
<tr>
<td>6. Are there clinically significant drug–drug interactions?</td>
</tr>
<tr>
<td>7. Are there clinically significant drug–disease/condition interactions?</td>
</tr>
<tr>
<td>8. Is there unnecessary duplication with other medication(s)?</td>
</tr>
<tr>
<td>9. Is the duration of therapy acceptable?</td>
</tr>
<tr>
<td>10. Is this medication the least expensive alternative compared to others of equal utility?</td>
</tr>
</tbody>
</table>

See reference 10 for more information.

Underuse of Medications

A third form of suboptimal drug use is underuse of medications.3 This may involve an undiagnosed and untreated condition (e.g., depression), a diagnosed condition but omitted treatment (e.g., beta blocker post-myocardial infarction [MI]), or the underuse of preventive treatment (e.g., calcium and vitamin D).21 Suggested causes for underprescribing in the elderly population may include clinicians’ fear of polypharmacy and risk of adverse drug reactions, age discrimination, and financial barriers for patients. Underprescribing in the elderly population may lead to increased morbidity, disability, and healthcare utilization and costs.21

Underuse detected by either implicit or explicit criteria has been shown to affect older adults in all clinical settings. An implicit measure known as the Assessment of Underutilization (AUO) has demonstrated good reliability and sensitivity to change in randomized controlled trials.22,23 One study of 196 older veteran outpatients taking over five medications found that 64% had evidence of medication underuse as determined by the AOU.5 The three most common drug classes that were underused were antihypertensives, anticoagulants, and lipid-lowering agents.5

The two most common explicit criteria for medication underuse in older adults are the Assessing Care of Vulnerable Elders (ACOVE) (Table 5-4) criteria24,25 and the Screening Tool to Alert Doctors to Right Treatment (START) criteria.9,23,26 The ACOVE criteria were developed by the RAND corporation as part of a large effort to educate clinicians and provide an evidence-based tool to assess the quality of healthcare of frail older adults. One study applying the START criteria to 600 hospitalized older patients found evidence of underuse in 57.9%.26 The most common types of underuse detected by the START criteria were statins in atherosclerotic disease, warfarin in chronic atrial fibrillation, and anti-platelet therapy in arterial disease.

**KEY POINT:** Suboptimal drug use is prevalent in older adults and is manifested as unnecessary, underused, or inappropriate medications.
**Table 5-4. ACOVE-3 Quality Indicators for Underuse of Medications**

<table>
<thead>
<tr>
<th>If This Is Present:</th>
<th>Consider Adding This:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Steroid therapy</td>
<td>Calcium + vitamin D + bisphosphonate</td>
</tr>
<tr>
<td>DM and proteinuria</td>
<td>ACEI and aspirin</td>
</tr>
<tr>
<td>Vaccination not contraindicated</td>
<td>Influenza, pneumococcal, tetanus toxoid, reduced diphtheria toxoid, and acellular pertussis (Tdap) vaccines</td>
</tr>
<tr>
<td>Opioid therapy</td>
<td>Laxatives</td>
</tr>
<tr>
<td>Peptic ulcer disease, high risk (75+; NSAIDs, steroid, warfarin use; or history of PUD/GI bleed)</td>
<td>Proton pump inhibitor or misoprostol</td>
</tr>
<tr>
<td>Atrial fibrillation</td>
<td>Anticoagulant</td>
</tr>
<tr>
<td>HF</td>
<td>ACEI, selective beta blocker</td>
</tr>
<tr>
<td>Chronic obstructive pulmonary disease</td>
<td>Inhaled long-acting bronchodilator/steroid</td>
</tr>
<tr>
<td>Stroke</td>
<td>Antithrombotic</td>
</tr>
<tr>
<td>HTN, HF, and IHD</td>
<td>Beta-blocker</td>
</tr>
<tr>
<td>HTN and either DM, HF, or chronic kidney disease</td>
<td>ACEI</td>
</tr>
<tr>
<td>IHD with myocardial infarction</td>
<td>Antiplatelet, beta-blocker, statin</td>
</tr>
<tr>
<td>Osteoarthritis</td>
<td>Acetaminophen</td>
</tr>
<tr>
<td>Osteoporosis</td>
<td>Bisphosphonate</td>
</tr>
</tbody>
</table>

ACEI, angiotensin-converting enzyme inhibitor; DM, diabetes mellitus; NSAIDs, nonsteroidal anti-inflammatory drugs; PUD, peptic ulcer disease; GI, gastrointestinal; HF, heart failure; HTN, hypertension; IHD, ischemic heart disease. See reference 25 for more information.

**Adverse Drug Events**

The term adverse drug reaction (ADR) implies a specific reaction usually related to the pharmacology of a drug, whereas an ADE is defined as any noxious, unintended, and undesired effect of a drug. In some studies, an ADE has been identified as any injury due to drug therapy. Therefore, ADEs are more encompassing and may include not only ADRs but also harmful adverse drug withdrawal events and therapeutic failures. Not all ADEs or ADRs are preventable, but if serious injury or death is the outcome of an ADE, an evaluation should be made to identify whether a change could reduce future likelihood of a similar outcome.27 Earlier literature tends to focus just on ADRs, whereas some recent studies evaluated ADEs that incorporated ADRs, adverse drug withdrawal events and therapeutic failures combined. When critiquing a publication or study, the specific definition being used should be clear, especially when comparing the incidence and prevalence of a drug-related outcome. The following epidemiology review includes studies focused on ADRs, studies focused on ADEs, and studies that have used overlapping terminology for ADRs and ADEs.

**Adverse Drug Reactions**

Epidemiologic studies of ADRs have generally focused on specific venues of care (e.g., nursing home, primary care, hospital) and show that ADRs are common in older adults. In a 4-year study of nursing homes, 67% of residents were found to have at least one probable ADR over the study time period.28 Another study of 335 nursing home residents found 207 ADRs via a retrospective chart review over a 1-year period.29 In a year-long, cohort study of community nursing homes in Massachusetts, 1.89 ADEs per 100 nursing home resident months were reported.30 A study of older adult primary care patients found that 14% had experienced an ADE within a 3-month period.31 This compares
Adverse Drug Withdrawal Events

Clinicians and investigators have reported numerous cases of adverse drug withdrawal events (ADWEs) and a few retrospective studies of this phenomenon in elderly patients. In a single nursing home in Texas, over an 18-month period, 62 patients experienced a total of 94 ADWEs (mean 0.54 per patient), corresponding to an incidence of 0.32 reactions per patient-month. The highest rate was found in another study of community-dwelling older adults who were just discharged from a hospital. In this study, 18.7% had at least one ADE within 45 days of discharge.

In a study of hospitalized elderly inpatients, 26% experienced an ADE, and 66% of the ADEs likely contributed to the admission. An observational study of hospitalized patients age 80 and above reported an incidence of 13%, of which 63% were considered preventable.

A meta-analysis of studies that evaluated ADRs and hospital admissions reported that older adults have four times the risk of an ADR-related hospital admission compared to younger patients. A majority of those ADR-related hospital admissions were considered preventable. A more recent retrospective cohort study in older veterans found that ADRs were associated with 10% of hospital admissions with 37% considered preventable.

Risk factors for ADRs in older adults include polypharmacy, multiple comorbidities, previous ADR, dementia, and the use of specific medications such as opioids, anticoagulants, anticholinergics, and benzodiazepines. In a study of nursing home residents, those taking nine or more medications were 2.33 times more likely to experience an ADR compared to those taking less than nine. In a community-dwelling study of older patients with mobility limitations, the number of drugs dispensed in the previous year was an independent risk factor for an ADR. In hospitalized older adults, comorbidity was associated with the risk of ADR in that there was a direct relationship between the Charlson Comorbidity Index and the risk of ADR.
cations (especially levodopa/carbidopa), benzodiaze­pines, and antidepressants.

Many of these previous examples were drug withdrawals resulting from a prescriber abruptly discontinuing an agent because it was deemed inappropriate or unnecessary or was suspected of causing an adverse event. Another area of concern is in transitions of care, in which discontinuation of medication could occur unintentionally for an elderly patient. One study of patients transferred from a nursing home to hospital and a hospital to a nursing home showed ADEs attributed to medication changes in 20% of patients; 50% of those ADEs were caused by discontinuation of a medication. The medications associated with an ADWE due to discontinuation were metoprolol, colchicine, metoclopramide, insulin, carbamazepine, and codeine. The study suggests that medication reconciliation is important in the prevention of ADWE in elderly patients.

Little is known about the risk factors for ADWEs. In the Texas nursing home study, ADWEs were associated with multiple diagnoses, multiple medications, longer nursing home stays, and being hospitalized. In primary care patients, the number of medications stopped was a significant predictor of ADWEs. Analyses reveal that the risk of an ADWE increased as the length of time off medication increased. It is important to note, however, that ADWEs rarely occur when medications are discontinued by tapering.

**KEY POINT:** Gradual dosage reduction should be attempted one drug at a time with a tapering dose, carefully observing the effect of each change. Documentation of the plan and results of previous drug withdrawals is important for any medical history.

**Therapeutic Failure**

Few data exist about the prevalence of therapeutic failure in older adults. Two studies used a reliable and valid 10-question causality algorithm, called the Therapeutic Failure Questionnaire, and reported that between 5% and 11.2% of hospital admissions in older U.S. veterans are due to an ADE. Among the most common conditions with therapeutic failure in both studies were heart failure and chronic obstructive pulmonary disease. Another study from Belgium showed that 8.2% of hospital admissions to a geriatric ward were due to drug therapy failure as measured by an implicit Likert scale measure. It is important to note that most cases of therapeutic failure reported by these studies were preventable and mostly due to medication nonadherence. Other reasons for therapeutic failure reported included lack of prescribing or too low a dose of an evidence-based drug.

**Reduction of Adverse Drug Events in Geriatric Patients**

Although many studies of clinical pharmacist interventions to improve drug therapy have been published, most are limited to specific drugs or disease states or are poorly controlled. There are few randomized controlled trials (RCTs) designed to reduce suboptimal drug use in older adults that have demonstrated ADE reductions. This discussion focuses on RCTs and systematic reviews.

One RCT of a clinical pharmacist intervention with 208 elderly outpatient veterans with polypharmacy showed that the rate of ADEs was lower in the intervention compared to the control group; 32.2% versus 40% (P = 0.19). Another RCT in 808 older veterans that compared outpatient care by a geriatric evaluation and management team to the usual care showed a 35% reduction in the risk of serious ADRs.

Three separate RCTs involving 1,184 elderly hospitalized patients showed that three different types of interventions (i.e., pharmacist drug regimen review, group patient education, and multidisciplinary education) all reduced ADE
readmissions. However, a systematic review of 21 descriptive studies and 10 controlled trials of clinical pharmacists providing medication reviews for patients of all ages at hospitals concluded that, despite variable study design and outcome measures, medication use, health services use, and costs were improved.

One RCT in nursing homes focused on warfarin demonstrated that a nurse intervention using Situation, Background, Assessment, and Recommendation (SBAR) to communicate with physicians led to an increase of international normalized ratio (INR) tests within the therapeutic range and a reduction in ADEs (although not statistically significant). However, a systematic review including both randomized and nonrandomized controlled studies in nursing home populations outside of the United States identified improved MAI scores, improved prescription of psychoactive medications, decrease in hospital usage, and fewer falls as evidence of the effect of pharmacist intervention on ADEs.

KEY POINT: A variety of interventions involving clinical pharmacy services and interprofessional education have been shown to reduce ADEs.

Opportunities to Reduce and Improve Drug-Related Problems in the Elderly

Medication Reconciliation

Medication reconciliation, which is defined by The Joint Commission as “the process of comparing a patient’s medication orders to all of the medications that the patient has been taking,” is another opportunity for pharmacists to reduce the risk for drug-related problems, particularly for patients moving from one venue of care to another. A medication reconciliation should be done whenever a patient is transferred between levels of care such as hospital admission and discharge, nursing home admission, or transfer to independent living. This is especially useful on discharge of a patient back to an independent living situation, because the institution’s medication formulary may be different from that of their Medicare Part D plan. Drugs from a similar class, or the same agent with a different dosage form, may have been started and need to be changed back to those previously taken at home.

In its most basic form, medication reconciliation is a comparison of one medication list to another, which is vital for identifying transcription errors and omissions. However, medication reconciliation provides an excellent opportunity for improving a patient’s pharmacotherapy. To perform a full review, additional data obtained from a medication history, medical records review, and/or the patient is necessary to match medications with their indications, clarify intended duration of therapy, or provide the rationale behind any intentional medication changes. Therefore, some healthcare settings employ enhanced medication review practices that incorporate these extra data.

Optimally, when a pharmacist is performing medication reconciliation he or she should also assess potential adverse effects and medication adherence or knowledge problems. This process is enhanced in the outpatient setting when patients bring in all prescription and non-prescription medications, including herbal and alternative therapies, to each healthcare visit. Additional probing may be needed to fully ascertain the extent of nonprescription product use (e.g., multivitamins, vitamin E, gingko biloba, ibuprofen, calcium carbonate) because patients, not believing them to be medications, may not voluntarily disclose these products to healthcare professionals.

KEY POINT: Optimal medication reconciliation should include more than just a comparison of drug lists.
Medication Therapy Management

Pharmacists can play a major role in resolving and preventing drug-related problems, especially suboptimal drug use with medication therapy management (MTM). MTM was adopted by the Center for Medicare & Medicaid Services as a recognized reimbursable service for beneficiaries of Medicare Part D. Regardless of the care setting, this process consists of the following steps: (1) taking a thorough medication history, (2) matching a patient's problem list with his or her medication history to detect potential over- and underuse, (3) assessing the appropriateness of the remaining drugs, and (4) making drug therapy recommendations to prescribers, other healthcare professionals, and patients to resolve any drug-related problems detected. Pharmacists conducting MTM may benefit from using a structured tool to improve efficiency and consistency. A recent review describes the various tools for assessment of inappropriate prescribing in the elderly patient, comparing those that may be helpful in daily practice, professional training, and research.

Using explicit criteria, the Tool to Improve Medications in the Elderly via Review (TIMER®) may help in the assessment of

- unnecessary use,
- underuse,
- inappropriate use (high-risk drugs),
- drug–drug and drug–disease interactions,
- medication nonadherence,
- attainment of therapeutic goals,
- medication cost and coverage, and
- ADRs, including those due to allergies.

Another helpful tool using implicit criteria is the MAI, which considers 10 domains (see Table 5-3) to evaluate each medication in a patient's regimen (described earlier in this chapter).

Step 1 for MTM is to identify the medications a patient is supposed to be taking. The medication history is usually obtained from the patient or caregiver and medical or pharmacy records. A medication reconciliation can provide the necessary medication list but may not be comprehensive (see Medication Reconciliation, above). After the pharmacist has an accurate and complete medication list for a patient, Steps 2, 3, and 4 are undertaken. Step 2 evaluates each medication to determine whether it is necessary for the patient. Each medication should correspond with one or more medical problems in the patient's past medical history or current problem list. Drugs that lack an indication may be unnecessary for the patient and should be evaluated to see whether they can be discontinued. Sometimes an indication exists but is not documented, and steps should be taken to clarify the intended indication. Drugs such as anticonvulsants, antidepressants, and corticosteroids should be tapered gradually to minimize a resurgence of an undocumented underlying condition, or withdrawal symptoms. In addition, it is important to evaluate whether drug therapy was prescribed to treat any adverse effects of another medication. An example of this prescribing cascade would be the use of levodopa to treat parkinson-like symptoms caused by metoclopramide. Another example of unnecessary drug use can occur in patients near the end of life. Chapter 6 provides a more detailed discussion of factors to consider at this stage.

Step 3 considers whether untreated medical conditions might benefit from evidence-based pharmacotherapy. For Step 4, the pharmacist must then evaluate whether the remaining drug therapy is appropriate. For example, a medication cannot be considered effective when the risks associated with drug therapy outweigh potential benefits. Another example of unnecessary...
sary medication is therapeutic duplication (i.e., two drugs from the same class). To assess proper dosing, the pharmacist should evaluate a drug’s pharmacokinetics and side effect profile and the patient’s renal and hepatic function. Patient preference and copay costs associated with the prescription drug plan’s formulary must also be considered. Other comorbid conditions and concomitant medications also need to be taken into account to avoid drug–disease or drug–drug interactions. Limiting the use of as-needed drugs and considering medications that can be dosed as few times per day as possible will help to enhance medication adherence.

After these steps of the MTM process are completed, a plan of care is developed, which must be communicated to be effective. It is imperative to communicate drug therapy recommendations to prescribers and other healthcare professionals to resolve any drug-related problems detected. In addition, patients in the ambulatory care setting and their caregivers should receive both written and verbal medication education to help to increase adherence. Considering generic options, utilizing compliance aids (e.g., pill boxes, medication calendars), and encouraging family support can help to improve medication adherence.63-65

MTM has evolved with the enactment of the Medicare Prescription Drug Benefit (Part D). In addition, MTM may further expand into new healthcare models, such as the medical home model and accountable care organizations. Provision of MTM by pharmacists has great potential to reduce drug-related problems in older patients.
CASE: **Suboptimal Drug Use and Adverse Drug Event**

**Setting:**
Inpatient ward.

**Subjective:**
WF is a 74-year-old man who saw his primary care provider because he noticed when he woke up that his “heart wasn’t beating right; it feels like it is going too slow.” WF denied chest pain, shortness of breath, nausea, or vomiting. He did note feeling dizzy earlier in the week. Six weeks earlier, WF was started on diltiazem CD 180 mg daily by his primary care physician to further lower his blood pressure to goal. His physician also at that time decreased the dose of his metoprolol tartrate from 75 to 50 mg bid. WF was sent to the hospital for admission.

**Past Medical History:**
HTN, T2DM, CAD s/p angioplasty 2 years ago, previous MI, EF = 60%, PVD s/p left femoral to posterior bypass, and history of one episode of atrial fibrillation (4 years ago).

**Medications on Admission:**
Digoxin 0.25 mg daily, diltiazem CD 180 mg daily, metoprolol tartrate 50 mg bid, lisinopril 20 mg daily, isosorbide mononitrate 30 mg daily, hydrochlorothiazide 12.5 mg daily, KCl 40 mEq every a.m., EC ASA 325 mg daily, warfarin 5 mg daily, famotidine 20 mg at bedtime, vitamin C 500 mg daily, insulin glargine 26 units subcutaneously at bedtime, insulin lispro 8 units subcutaneously with meals, vitamin E 400 international units daily, ibuprofen 200 mg two tablets as needed for pain (takes at least one dose per day), multivitamin daily, calcium/vitamin D 500 mg/200 international units twice daily.

**Physical Examination:**
BP 110/50 mmHg, P 38 BPM, RR 24. The rest of the physical examination is unremarkable.

**Labs:**
Potassium 6.9 mEq/L, serum creatinine 1.9 mg/dL (baseline 1.2 mg/mL), BUN 35 mg/dL, fasting glucose 102 mg/dL, WBC 5800/mm³, hematocrit 35%, digoxin level 2.78 ng/mL, INR 2.3.

Electrocardiogram: bradycardia with normal sinus rhythm.

Hospital course: WF was admitted to the coronary care unit and received sodium polystyrene sulfonate for increased potassium; digoxin, diltiazem, and metoprolol were held, but all other home medications were continued. Over the next few days, his heart rate and blood pressure increased to 82 BPM and 145/85 mmHg, respectively. WF was transferred to the geriatrics evaluation and management team and restarted on metoprolol for hypertension and coronary artery disease. The pharmacist on the geriatrics team was asked to review the patient’s home medications for appropriateness. After interviewing the patient and reviewing the records, the pharmacist provided the following medication assessment and plan.

**Assessment:**
1. Hospital admission secondary to medication-related adverse events: Use of multiple agents to treat hypertension without titration to maximum dose, use of digoxin and warfarin without current indication, use of NSAID despite current diagnosis and treatment of HTN, and use of potassium chloride supplementation in the presence of an ACEI.
2. Home medications without a current indication for use in this patient: famotidine, warfarin, digoxin, vitamin C, and vitamin E.
3. Patient with significant cardiac history and DM without assessment or treatment for hyperlipidemia.

**Plan:**

1. Discontinue famotidine, diltiazem, digoxin, warfarin, vitamin C, and vitamin E due to lack of a current indication for use.
2. Reduce dose of ASA to 81 mg to reduce the risk of gastrointestinal bleeding.
3. Titrate metoprolol and lisinopril for a blood pressure goal of <140/90 mmHg.
4. Re-evaluate need for hydrochlorothiazide in addition to two other antihypertensive agents as they may be less effective in patients with reduced renal function (i.e., <30 mL/min).
5. Re-evaluate need for KCl in light of increasing lisinopril dose and possible discontinuation of hydrochlorothiazide.
6. Re-evaluate need for multivitamin. If the patient is eating a well-balanced diet, these supplements may be discontinued with little risk but with the benefit of a decreased pill burden.
7. Change from ibuprofen to acetaminophen for headaches, as ibuprofen may worsen HTN, renal function, and risk of PUD with aspirin.
8. Order cholesterol panel and evaluate patient for statin therapy.
9. Refer to geriatric evaluation and management clinic pharmacist for medication therapy monitoring as an outpatient.

**Rationale:**

1. This patient is a classic example of polypharmacy, evidenced by unnecessary drug use, because several of his prescribed and OTC medications have no currently active medical indication. In addition, multiple drugs were prescribed at less than maximum doses for treatment of hypertension, increasing the pill burden and risk for drug-related problems. The digoxin dose is higher than recommended by the Beers’ criteria for an older adult, and the addition of diltiazem at the last office visit likely further elevated the digoxin serum concentration. Digoxin toxicity was further increased by the high serum potassium level, which was a result of potassium supplementation along with use of an ACEI.

2. Furthermore, another form of suboptimal drug use may be present in the underuse of a cholesterol-lowering medication, which is likely in this patient with a long history of cardiovascular disease.
Clinical Pearls

• Transitions in care are crucial periods in which drug therapy may be changed; medication reconciliation is needed to prevent ADEs. Often, agents are added when a patient is in the hospital but the drug may not be needed long term. Also, chronic medications are sometimes changed due to formulary restrictions. Some good examples are proton pump inhibitors and $H_2$ blockers, which are frequently added with hospitalization or changed to the formulary product. At discharge, medication reconciliation that incorporates steps to identify these changes will reduce the risk for a patient to return home with duplicate therapy (i.e., taking both the medication used in the hospital and the chronic medication used at home), unnecessary drug therapy (i.e., an acid suppressant to prevent stress ulcers that is no longer indicated), or expensive medication not covered by the patient’s Medicare Part D formulary (i.e., prescription proton pump inhibitor instead of an OTC product).

• Information about OTC agents and herbal products are necessary pieces of information for a complete medication history. To obtain this information, ask questions about what the patient uses to treat complaints he or she has. For example, What do you take when you get a headache? This helps prompt the patient to think about all of the OTC agents he or she uses daily.

Chapter Summary

Older adults often need multiple medications to treat their conditions. Due to complex medication regimens, suboptimal drug use is prevalent. Pharmacists are crucial in detecting suboptimal prescribing and ADEs and in the use of MTM to provide the most effective care for patients.

Self-Assessment Questions

1. What are important factors when evaluating a medication for an older adult?

2. TJ is an 88-yo male who was treated for a major depressive episode for the past year. He is no longer depressed, and his medication was abruptly discontinued. He starts to experience vertigo, malaise, fatigue, and alteration in sensations. What drug-related problem is TJ experiencing?

3. What are some examples of suboptimal drug use?

4. What evaluations may be used to determine unnecessary medication use?

5. What tools use implicit criteria to determine medication appropriateness for older adults?

References


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Palliative and Hospice Care

LINDSEY DAYER and LISA C. HUTCHISON

Learning Objectives

1. Contrast the terms palliative care, comfort care, and hospice care.
2. Describe the goals of care in the dying geriatric patient.
3. Assess common symptoms in the dying geriatric patient.
4. Design a drug therapy plan to manage a geriatric patient at different stages of dying.
5. Discuss grief and bereavement.

Key Terms and Definitions

COMFORT CARE: Palliative care that is provided once a patient has decided to forego curative, aggressive interventions.

HOSPICE: A system to provide pain and other symptom management, which also includes psychological and spiritual aid, to terminally ill patients with a prognosis of 6 months or less.

PALLIATIVE CARE: The active, total care of patients whose disease is not responsive to curative treatment.

PROPORTIONATE PALLIATIVE SEDATION: Increasing sedation with the goal of controlling symptoms intractable to other management modalities.

SPIRITUALITY: The search for meaning and purpose in life and in the present moment.

TERMINAL SECRETIONS: Oral secretions that accumulate in the last days or hours of life as a patient loses the ability to swallow. When air passes through the accumulated secretions, a gurgling or rattling sound is heard, frequently called the “death rattle.”
**Introduction**

Despite efforts for more than 30 years, significant misconceptions persist about death and dying as they relate to older adults and to the healthcare system. Older adults frequently express anxiety regarding the process of dying but prove generally accepting of death itself. This anxiety most likely stems from concerns that death will be characterized by pain, suffering, loss of independence, and loneliness. Many patients in this situation fear that they will no longer receive the necessary symptom control because the healthcare system is geared toward treatments that cure. Compared to community-dwelling older adults, individuals in long-term care institutions express more fear, perhaps arising from higher levels of dependence on others, lower self-esteem, and loss of purpose in life. In general, the youngest old are similar to younger adults in their approach to death and dying. The oldest old begin to face death differently, perhaps because of increased frailty and dependence. This chapter will review end-of-life concerns, the hospice model of care, and specific pharmacologic and nonpharmacologic issues associated with the end of life and bereavement.

**Death and Dying**

Many people, including healthcare professionals, are not aware of what to expect as a patient progresses through the months prior to death, or within the last days or hours of life. Although millions of people die each year in the United States, mostly from chronic illness, this gap in knowledge stubbornly persists. Reduced mortality rates and changes in where one dies (e.g., hospital, nursing home) have removed the average American from exposure to the process. Patients and family members are torn between fear of what is to come and a desire to understand it. Information about illness and its progression that also includes guidance about symptoms to expect and how to manage them proves helpful in allaying these fears. Pain, depression, and anxiety are usually observed early on for patients at the end of life, whereas other symptoms (fatigue, anorexia) develop later. But an individual's death and dying involve experiences beyond the physical and psychosocial. Therefore, the models of care and support to aid in achieving a “good” death must address spiritual experiences as well as life closure, death preparation, and grief.

Discussing end-of-life issues with patients and family is thought to help reduce death anxiety. However, healthcare providers find this to be challenging, and few providers receive adequate training to feel comfortable addressing treatment decisions, future symptoms, and preferences for death. Simply knowing how to start the discussion offers a place to begin learning about treatment of the dying patient.

Exploring fears and dispelling myths is a good first step toward reassurance. For example, a patient may assume that the process of death will be similar to that observed in someone else. Family members may have concerns over whether they are capable of meeting the needs of their loved one if he or she prefers to die at home. Patients need to be given information about these issues as well as the time to evaluate treatment decisions and determine preferences. If possible, it is best to have discussions about death and dying over several visits, to encourage patients to develop a trusting relationship with their healthcare provider.

Pharmacists are not the typical healthcare professionals who identify a patient's wishes regarding the overall dying process. However, whether the pharmacist is dispensing medications, performing rounds within a hospital, consulting in a nursing home, or practicing in hospice or palliative care settings, he or she will have the opportunity to assess and counsel dying patients. A careful approach that recognizes the process of death is warranted, because missteps could hinder progress in helping a patient cope and adapt to the situation. Providing pharmaceutical care to this population
requires the pharmacist to understand spiritual considerations as well as social and community influences on an individual patient. The ability to identify and assess symptoms of a palliative care patient with regard to the patient’s emotional, mental, and social state aids in making the best treatment decisions. The pharmacist has an integral role in discussing symptom management and pharmacotherapy with the patient.\(^5\)

It is helpful to understand cultural differences in the approach to death and healthcare decision making associated with the end of life in order to place a patient’s desires for symptom control and pain relief in context. Table 6-1 identifies several cultural groups and how older adults from them frequently approach healthcare decision making, as well as common difficulties encountered by healthcare professionals.\(^6\) However, each cultural group is composed of people from a wide range of backgrounds, and an individual may be a member of a cultural group but hold different attitudes and beliefs. Although it is helpful to understand ethnic patterns in general, the pharmacist must identify the desires of the individual patient, which may not follow those patterns.

### End-of-Life Care

End-of-life care can be a confusing term because multiple definitions, components, and systems of delivery exist. The term initially referred to healthcare that is provided in the final days or hours of life but has been expanded to include care for any patient with an illness or condition that is progressive and incurable. Palliative care, comfort care, and hospice are components of end-of-life care. Palliative care strives to reduce symptoms and anxiety associated with a disease to ensure the best achievable quality of life as the disease progresses. It is intended to encourage patients to live actively while neither hastening nor postponing the time to death. As such, palliative care can be offered to individuals living with a complex, chronic disease whether or not they are expected to recover. Palliative care that is provided when a patient has decided to forego curative, aggressive interventions is termed comfort care. Although both palliative and comfort care aim at symptom relief, palliative care does not indicate that potentially curative treatments have been stopped.

### Table 6-1. Common Cultural Differences in Healthcare and End-of-Life Decision Making

<table>
<thead>
<tr>
<th>Cultural Group</th>
<th>Communication About Healthcare Decisions</th>
<th>End-of-Life Decisions</th>
</tr>
</thead>
<tbody>
<tr>
<td>African American</td>
<td>Family usually involved</td>
<td>Aggressive therapies usually favored</td>
</tr>
<tr>
<td></td>
<td>Fictive kin (individuals not related by blood or marriage) also consulted</td>
<td>Resistant to DNR orders</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Clergy support welcomed</td>
</tr>
<tr>
<td>Native American</td>
<td>Close and distant relatives involved</td>
<td>Avoid life expectancy predictions; considered self-fulfilling</td>
</tr>
<tr>
<td></td>
<td>Considered rude to interrupt</td>
<td>Desire for unfettered struggle with death</td>
</tr>
<tr>
<td></td>
<td>Pauses to assure speaker is finished</td>
<td>Desire to stay in homeland</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Desire to remain hopeful, positive</td>
</tr>
<tr>
<td>Asian Indian</td>
<td>Emphasis on interconnectedness</td>
<td>Prefer to die at home</td>
</tr>
<tr>
<td></td>
<td>Family and friends consulted</td>
<td>May have important rituals with dead body</td>
</tr>
<tr>
<td>Chinese American</td>
<td>Decisions made by family</td>
<td>Critically ill patients prefer hospitalization</td>
</tr>
<tr>
<td></td>
<td>Older men take primary role</td>
<td>Speaking about death considered bad luck</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Preference for physician to make decisions</td>
</tr>
<tr>
<td>Latin American</td>
<td>Family takes priority</td>
<td>Family, physician, and religion influences</td>
</tr>
<tr>
<td></td>
<td>Focus on present, not future</td>
<td>Aggressive treatment usually favored</td>
</tr>
<tr>
<td></td>
<td>May only make decision in family group setting</td>
<td></td>
</tr>
</tbody>
</table>

DNR, do not resuscitate.
For additional information, see reference 6.
Hospice care as a distinct modern concept originated in Great Britain as a system to provide pain management and other symptom relief that also includes psychological and spiritual aid for terminally ill cancer patients. However, patients with any terminal disease will benefit. Typical non-cancer diagnoses are end-stage organ disease (e.g., dementia, congestive heart failure [CHF], chronic obstructive pulmonary disease [COPD]), and unspecified debility. In the United States, hospice care is a program paid for by Medicare Part A, Medicaid, and private insurance for beneficiaries with a prognosis of 6 months or less. More than 42% of hospice patients receive care at home, 24% receive care in a nursing home or residential facility, and 26% receive care at an inpatient hospice facility. An interprofessional team of physicians, nurses, pharmacists, social workers, chaplains, home aides, and volunteers provide needed care for the patient and education and bereavement counseling to family and friends.

**KEY POINT:** Hospice is not a place. Palliative and hospice care can be provided in any setting: home, assisted living facility, nursing home, or hospital.

In the past, hospice did not pay for medications unrelated to the hospice diagnosis, nursing home residential costs, or any curative treatments. If a patient needed those items, he or she would pay out of pocket, through other insurance (e.g., Medicaid for nursing home costs), or convert out of the Medicare Hospice Benefit back to original Medicare or Medicare Advantage. However, due to potential overpayments and fraud between the hospice benefit and Medicare Part D coverage, regulations were changed so that any prescriptions submitted through Medicare Part D for a beneficiary enrolled in hospice would be denied coverage, requiring the hospice provider to ensure they had not already covered the cost. This was meant to remove ambiguity and reduce overlapping expenditures, reported as $33 million in 2009. This change may delay receipt of medications that were previously covered by Medicare Part D while current coverage is being confirmed.

**Common Nonpharmacologic Issues in Palliative Care**

In developed countries, most end-stage chronic illness occurs in individuals over age 65, and death from these illnesses is preceded by physical and functional disability. Caring for elderly patients with chronic disease is medically and ethically challenging, and hospice and palliative care is especially useful. The first issue in palliative and hospice care is for a patient and his or her physician to discuss the end of life, so the patient can make better decisions about care. Having these forthright discussions should not make a patient sad, worried, or terrified. A standard list of questions may be helpful to initiate discussion:
• What is my chance of cure?
• Will I live longer with treatment?
• What are the side effects of treatment?
• Are there other options?
• Are there any clinical trials available? Am I eligible?
• What are the likely things that will happen to me with this disease?
• How long will I live? (Ask for a range.)
• Are there things I should be doing for my family, or financial concerns?
• Who is available to help me cope with this situation?

Whereas some clinicians and family fear that confronting end-of-life issues may cause a newly diagnosed patient to lose hope, most patients want to discuss their illness and wishes as well as the advantages and disadvantages of treatment because it results in better decisions and a greater sense of control. Such discussions can improve quality of life and reduce family bereavement.13

Part of the end-of-life discussion identifies goals of care and the wishes of the patient and family regarding treatment. Life-prolonging or disease-modifying treatments should be explained, outlining the positive and negative consequences that may occur given the patient’s current status. Improving a patient’s quality of life is usually an appropriate goal throughout the disease process, whether achieved through pharmacologic or nonpharmacologic means. The goals of care should include a specific discussion about pain management. Pain is a known symptom of cancer, but many clinicians do not realize that 50% to 85% of advanced COPD and CHF patients also report pain symptoms.13 Quality-of-life goals should also address symptoms such as nausea, constipation, fatigue, dyspnea, anxiety, and depression. Complex psychosocial and spiritual issues should be addressed, in goals of care.

In late stages of disease, invasive or intensive therapies associated with life-prolonging outcomes (e.g., admission to an intensive care unit, ventilation, resuscitation, chemotherapy, use of a feeding tube) may not necessarily extend survival.11,13 A major study compared cancer patients with a 3-year prognosis who received hospice and no chemotherapy to patients who did not receive hospice care but did receive chemotherapy. The study showed survival was significantly longer or no different for hospice patients, depending on the type of cancer.12 Individuals admitted to hospice for more than 1 week report an improved quality of life compared to those not in hospice care.11 At late stages of disease, the goals of care should be discussed and modified as appropriate for the patient and his or her values. This can be a complex task, especially if the patient or family does not understand the prognosis. Involving palliative care physicians and team members at an earlier stage may enable trusting relationships and improved communication with older adults because the team members will already be part of the individual’s care.

A second issue comprises personal values, such as spirituality and dignity, which may be overlooked at the end of life. As death approaches, spiritual concerns can be as important as physical symptoms for the patient. Hospice services include clergy or other bereavement counselors.8 Patients may feel a loss of dignity when they are unable to perform familiar tasks (e.g., taking care of others, living in an independent and self-directed manner, being mentally alert). It is important for pharmacists to be aware of such issues when interacting with patients and their families. There is limited evidence regarding the appropriate role of pharmacists in spiritual assessment and care. Nevertheless, data from nursing and physician roles may guide pharmacists involved in direct patient care.14 One study examined 156 patients with cancer and found that 42% wanted their nurse to enquire about their spiritual beliefs. Of those, 66% wanted their nurse to offer to pray
privately for them, and 41% wanted their nurse to pray with them.\textsuperscript{15} Some general strategies are available to address spiritual issues and may not require additional training.\textsuperscript{16} One of the most important strategies is to listen to and empathize with the patient. If the patient wishes, refer to a chaplain or invite clergy from the patient’s religious practice to meet with him or her.\textsuperscript{16-18}

KEY POINT: Address spiritual concerns, as well as physical symptoms, in order to provide the patient with a better quality of life as death approaches.

A third issue in palliative care is symptom assessment. Although considered a nonpharmacologic intervention, it is imperative that assessment be done well to adequately guide pharmacotherapy for a patient. As described in Chapter 4, evaluating older adults (compared to younger adults) means being on the lookout for specific nuances. Some hospice programs may use specific validated assessment tools to identify the presence and intensity of symptoms; others select tools related to the patient’s diagnosis. Examples of assessment tools include the Edmonton Symptom Assessment Scale, which addresses a variety of common symptoms at the end of life, and the Geriatric Depression Scale. Examples of tools that focus on the patient’s diagnosis include the Functional Assessment Staging Test (used to measure the course of Alzheimer disease) and the New York Heart Association Functional Classification for patients with heart failure.\textsuperscript{19} In elderly and younger patients, physical pain is the most common complaint.\textsuperscript{20} In older adults, symptom burden is high and frequently under-recognized. In addition to symptom assessment, functional assessment is important in the older adult. As disease progresses, the patient may lose independence, increasing physical and psychological needs.

Additional challenges may exist in evaluation of a patient who has significant cognitive impairment. These patients may not remember pain or other symptoms experienced 24 hours prior and are only aware of current complaints. If severe cognitive impairment is present, patients who are nonverbal may express pain or other symptoms through facial expressions, mental status changes, changes in activity, interpersonal interactions, or specific body movements (guarding, fidgeting, pacing, or decreased mobility).\textsuperscript{21}

Finally, caregiver burden should not be underestimated. As described in Chapter 1, informal caregivers generally have increased responsibility as a patient grows more dependent, which may lead to stress, fatigue, and poor health outcomes. Hospice programs provide support, with instructions on how to care for the patient, short-term respite care, and bereavement services.

Common Pharmacologic Issues in Palliative Care

A multimodal approach to symptom management is of utmost importance, especially in the frail and elderly patient. Elderly patients are more sensitive to medications; by utilizing other members of the interprofessional team (e.g., social workers, chaplains, psychologists), inappropriate medications may be avoided and excessive use of medications may be decreased. After a thorough patient assessment, the choice of medication is dependent on many elements including symptom severity, ongoing disease states, goals of therapy, and availability and cost of therapy.

Pharmacokinetic Changes

In addition to the many pharmacokinetic and pharmacodynamic changes occurring in older adults that may impact response to drug therapy, other factors include frailty and the effects of disease in the patient who is approaching the final chapters of life.\textsuperscript{22-26} It is appropriate to start with the most basic pharmacokinetic changes. Oral absorption may be impaired by nasogastric suction. Further slowing of contractions in
the gastrointestinal (GI) tract may occur due to treatment with opioids. If the end of life is particularly stressful physically or psychologically, an increase in acid production may occur, increasing the risk for ulceration, especially if nonsteroidal anti-inflammatory drugs (NSAIDs) are employed.27

Volume of distribution is another pharmacokinetic dimension that may be altered if the patient has edema or third-space accumulation of fluid. Serum albumin concentrations may decrease if hepatic function is diminished or protein intake reduced. The resulting reduction in protein binding can significantly increase free drug concentrations in the blood, causing toxicity even at normal doses.27

Significant pharmacokinetic alterations can also alter elimination of drugs from the body. Fever and inflammation may decrease cytochrome P450 (CYP450) oxidative metabolism, particularly during end-stage liver disease. The CYP subfamilies 1A2, 2E1, and 2D6 may be significantly affected, either down-regulated or up-regulated depending on the patient’s disease and ethnicity. CYP enzyme derangements can drastically increase or decrease rates of drug elimination, with predictable harm to the patient. Glucuronidation enzymes are generally preserved in the liver. If not preserved, then extrahepatic glucuronidation enzymes in the kidney and gut compensate for any decrease. Kidney excretion can be estimated using creatinine clearance but has the same caveats as found in all older adults.27

**Dosage Forms**

When choosing a dosage form for a medication, factors to consider include best route of administration, dosing frequency, cognitive state of the patient, and physical impairments. Oral administration is simplest and usually preferred; however, if a patient is unable to swallow solids, then oral liquid, sublingual, parenteral, rectal, or transdermal routes must be used. As a patient becomes unable to swallow a solid dosage form, a rapidly dissolving or sublingual tablet may be substituted, if available. In many instances tablets may be crushed, or capsule contents added to jelly or applesauce. Of course, certain medications cannot be crushed. Compounded oral solutions may be prepared for some medications if point-of-care preparation is not feasible.28

Commercially available transdermal products offer another convenient method to administer medications, and this route often provides a sustained release so dosing intervals can be extended. Another option in palliative and hospice care is to have topical dosage forms compounded for administration; however, this should be limited to medications with proven transdermal absorption. For example, a compounded formulation of lorazepam, diphenhydramine, and haloperidol was a common choice by many centers for treatment of nausea and vomiting.29 Nevertheless, a pharmacokinetic evaluation showed absorption insufficient to cause any effect, and a trial demonstrated anti-nausea effects to be similar to placebo.30,31 Localized neuropathic pain that will not respond to topical application of commercially available products (e.g., lidocaine patch) may respond to compounded N-methyl D-aspartate (NMDA) antagonists, clonidine, or doxepin for topical use.32

**Tailoring Medication Appropriateness in Palliative and Hospice Care**

Hospice care originated with the need for more effective pain and symptom control in cancer patients at the end of life. In the past, too few medications were being used to sufficiently ease suffering. Only recently have providers begun to recognize that for patients at the end of life medication appropriateness should be assessed to reduce pill burden and exposure to medications that are unlikely to provide clinical benefit to patients with limited life expectancy. Prescribing has been traditionally guided by evidence from randomized controlled clinical trials, on which guidelines are based. However, most clinical trials for medications used in chronic progressive disease would exclude individuals who
are nearing the end of life. Medication use in a patient with reduced life expectancy should incorporate an added layer of scrutiny.\textsuperscript{33}

Efficacy and safety are still paramount in identifying appropriate medications for use in an older adult near the end of life. The clinician must also consider whether the expected therapeutic outcomes can reasonably be achieved within the patient’s estimated life expectancy. The difficulty in discontinuation of medication is illustrated by several statistics. Insurance claims for potentially inappropriate medications used during the last year of life revealed that 44\% of Medicare Advantage members received one such drug.\textsuperscript{34} Statins were continued in over half of Veterans Administration patients during the last 6 months of life.\textsuperscript{35} Among patients enrolled in hospice for end-stage dementia, 21\% were prescribed cholinesterase inhibitors and memantine.\textsuperscript{36}

\textbf{KEY POINT:} The goals of care change for patients closer to the end of life and no longer follow treatment guidelines for prevention or cure of illness.

A model has been proposed for evaluating the appropriateness of medication use in older adults. The patient’s life expectancy is estimated using life tables or multidimensional models designed for use with specific illnesses or functional states.\textsuperscript{33} Next, the likely time until the benefit of the medication is achieved is compared to life expectancy. For example, opioids for pain management tend to have a rapid onset of action, within minutes to hours. This compares to preventive medications (i.e., antihypertensives) which may require months or years for clinical benefit to occur. Should a patient have a relatively short life expectancy, preventive medications may not have time to achieve expected outcomes. Other components of the model are goals of care and treatment targets, which are paramount in determining a treatment plan and may negate any practice guidelines. When goals of care are established, treatment targets can be identified. These targets become the elements of the plan of care, with goals of care, life expectancy, and time to benefit used to tailor the choice and implementation of treatment.\textsuperscript{37}

\textbf{Re-evaluating Potentially Inappropriate Medications}

Often, medications that would normally be considered inappropriate in older adults may be suitable for geriatric patients in the palliative care setting. What may customarily be considered a side effect of a medication becomes a therapeutic benefit. Some agents have worrisome effects in patients who are expected to live months to years more but may not be an issue in those who only have days or weeks left to live.\textsuperscript{39} For example, dry mouth from scopolamine patches, usually an undesirable effect, is helpful to reduce secretions at the end of life. Long-acting benzodiazepines may be preferred in a patient who is bed-bound and unlikely to fall.

To review the use of medications in patients approaching the end of life, especially in the elderly, the questions in Table 6-2 can be considered, which help with the effort to optimize therapy and decrease adverse effects.\textsuperscript{39} It has been shown that when patients are initially referred to palliative care, as many as 20\% are already receiving at least eight other medications, usually for comorbid conditions.\textsuperscript{40-42} The risk for adverse drug reactions and medication interactions increases when more medications are taken. It is estimated that the risk of adverse drug interactions is more than 80\% when more than seven medications are taken on a regular basis.\textsuperscript{43} Because many pathophysiologic changes may affect metabolism, excretion, and volume of distribution of the chronic medications for comorbid conditions in the setting of a life-limiting illness, it is important to review a patient’s medications to ensure appropriateness of each medication.\textsuperscript{44} New medications will usually be introduced for symptom control as the patient’s life-limiting illness progresses, and these additions all increase the risk for medication interactions and adverse drug events. At the end of life, priority shifts from prolonging a patient’s
life to improving quality. If a patient is receiving medication that offers no benefit in quality of life, consider discontinuing the agent.

Discontinuation of medication in patients near death is a process similar to initiating drug therapy. First, an indication to discontinue medication must be identified. As goals of care change and patients become more frail, an increased risk for harm from a medication may develop. In addition, the drug may be identified as providing no clinical benefit. Communication with the patient and/or family must occur to ascertain their understanding of the medication’s benefits and harms, and to address what objections they may have toward discontinuation. Empirically, it is best to stop one drug at a time, in a manner that will minimize any adverse drug withdrawal events. For some agents, such as aspirin or warfarin, there may be no physiologic withdrawal symptoms. For others, such as digoxin or diuretics, there may be risk for exacerbation of an underlying condition. A third category would be medications such as beta blockers or antidepressants, which cause rebound or withdrawal symptoms. Whatever type of agent is discontinued, the patient should be monitored for adverse effects. With drugs that cause physiologic withdrawal, or where exacerbation of an underlying condition may cause additional symptoms, it is best to taper to the lowest doses before discontinuation, to minimize the risk to the patient.

**KEY POINT:** At the end of life, priority shifts from prolonging a patient’s life to improving the quality of it. If a patient is receiving medication that offers no benefit in quality of life, discontinuing the medication may be beneficial.

**Pharmacologic Management of Symptoms**

Many symptoms and signs may occur in the actively dying patient. They vary depending on the patient and the length of time before death occurs. Symptoms that may be present earlier in the dying process (i.e., months left to live) include pain, constipation, and anxiety and depression. In the weeks before death, patients may experience nausea and vomiting, anorexia, and fatigue. In the actively dying patient (i.e., days left to live), dyspnea, agitation, decreased levels of consciousness, changes in breathing, and other symptoms listed in Table 6-3 may be present. The sections below will discuss many of these symptoms and their pharmacologic management; however, evidence is sparse for effective management of symptoms in the elderly. Nonpharmacologic measures are not specifically addressed in this chapter, although the best care for elderly patients at the end of life is a combination of pharmacologic and nonpharmacologic measures.

**Symptom Management**

**Pain Management**

Pain can be one of the most difficult and distressing symptoms to manage in the elderly. For elderly patients at the end of life, it is important to remember the concept of “start low and..."
go slow.” It is equally important to “get there” (i.e., adequately relieve pain). Although there is a higher rate of adverse effects with opioids in this patient group, there is also a higher rate of undertreated individuals. Accurate pain assessment is vital in determining the best treatment plan for the patient (see Chapter 4). For patients who cannot verbally describe their symptoms, nonverbal pain scales and attentive patient assessment are important.

Some medications are specific to the end of life and palliative care. Non-opioid pain management is commonly used for mild to moderate pain as well as in specific types of pain (e.g., bone pain). Classes of medications or agents in

Table 6-3. Signs Present when Death Is Imminent

<table>
<thead>
<tr>
<th>Clinical Sign</th>
<th>Additional Information</th>
<th>Management</th>
</tr>
</thead>
<tbody>
<tr>
<td>Weakness and fatigue</td>
<td>Monitor for pressure ulcers.</td>
<td>Reposition the patient to prevent pressure ulcers.</td>
</tr>
<tr>
<td>Decreased food and fluid intake</td>
<td>May occur earlier in the terminal disease; however, when death is imminent, patient is usually not hungry. Forcing food and fluids may cause discomfort. Dehydration occurs naturally in the dying.</td>
<td>Moisten and care for the mouth, nose, and eyes by moistening and cleaning the mouth, coating the lips and anterior nasal mucosa with petroleum jelly, and moistening the conjunctiva with an ophthalmic lubricant if the eyes are not closed.</td>
</tr>
<tr>
<td>Decreased ability to swallow and cough</td>
<td>May lead to noisy breathing (gurgling, crackling, and rattling).</td>
<td>Refer to the section Terminal Secretions.</td>
</tr>
<tr>
<td>Reduced circulation and renal function</td>
<td>Occur due to dehydration and decreased cardiac output. May cause the extremities to look cyanotic and feel cool when touched.</td>
<td>None. Intravenous fluids will not reverse the decreases in organ function at the end of life and may cause other problems (e.g., fluid overload).</td>
</tr>
<tr>
<td>Decreased levels of consciousness</td>
<td>Encourage family and friends to talk to the patient, who may still hear and sense their presence.</td>
<td>None.</td>
</tr>
<tr>
<td>Agitation</td>
<td>Mild symptoms may respond to soft music or calming, comforting words.</td>
<td>Refer to the sections Agitation and Delirium and Proportionate Palliative Sedation for management of more complicated symptoms.</td>
</tr>
<tr>
<td>Incontinence</td>
<td>Educate family members regarding loss of bladder and bowel function, and demonstrate how to address it.</td>
<td>Manage based on symptom (e.g., urinary incontinence vs. bowel incontinence)</td>
</tr>
<tr>
<td>Changes in breathing</td>
<td>May present as periods of apnea, irregular patterns of respiration, or Cheyne-Stokes–pattern tachypnea</td>
<td>Refer to the section Dyspnea for management of breathlessness.</td>
</tr>
<tr>
<td>Loss of ability to close eyes</td>
<td>Explain to family members that this is common.</td>
<td>Continue to moisten the conjunctiva with ophthalmic lubricants or artificial tears.</td>
</tr>
<tr>
<td>Near-death awareness</td>
<td>Patients may appear to describe what dying is like; it may be difficult to distinguish between a near-death awareness and delirium.</td>
<td>Involve a multidisciplinary team to offer support for the family.</td>
</tr>
</tbody>
</table>

For additional information, see reference 16.
this category include NSAIDs, acetaminophen, steroids, and bisphosphonates (see Table 6-4). Corticosteroids are often used in those who are terminally ill for symptoms such as bone pain and visceral pain (e.g., obstruction), among others. It is common to encounter corticosteroid treatment at the end of life. Dexamethasone is the most frequently used corticosteroid and is considered the drug of choice. It causes less sodium and fluid retention than other agents in the class. It has a long half life (>36 hours) and, therefore, can be given once a day. Short-term courses of corticosteroids rarely cause the side effects associated with long-term use. Still, a reversible delirium known as steroid psychosis may develop, especially in elderly patients. Bisphosphonates and other bone modifying agents (denosumab) may be used for relief of bone pain. These have also been shown to decrease the time to skeletal-related events (e.g., fractures) in patients with bone metastases. These are unlikely to be covered under the patient's insurance in the hospice setting, even though they may be beneficial in palliative care.

Opioids are the most useful and flexible agents for treatment of pain in patients at the end of life. They are recommended by the American Geriatrics Panel on the Pharmacological Management of Persistent Pain in Older Persons, regardless of whether patients are at the end of life. Opioids should always be considered in patients with moderate to severe pain. In the palliative care setting, immediate-release opioids may be prescribed based on the peak effect of the medication, rather than the duration of action. For example, morphine immediate release may be prescribed every 1–2 hours as needed for pain instead of every 4 hours, which is the duration of action of immediate-release morphine. If a patient is unable to swallow, some alternatives include sublingual administration of concentrated morphine solution, oxycodone immediate-release solution, off-label administration of sustained-release morphine, or oxycodone given rectally.

Adjuvant analgesics may be beneficial in some patients, especially those experiencing neuropathic pain. The most common adjuvant analgesic classes for the treatment of neuropathic pain are the anticonvulsants, tricyclic antidepressants (TCAs), serotonin norepinephrine reuptake inhibitors (SNRIs), and topical local anesthetics. These medications must be started at low doses and titrated slowly to avoid potential side effects. Therefore, it may take up to 2–3 weeks for onset of the full effect. Estimating the amount of time a patient has left before death may help decide whether an adjuvant analgesic would benefit the patient. Table 6-4 lists specific adjuvant analgesics to consider for these patients.

Angina is another type of disease-specific pain. Medications used to treat and/or manage it should be considered, including nitrates, beta blockers, calcium-channel blockers, and ranolazine.

**KEY POINT:** Pain can be one of the most difficult and distressing symptoms to manage in the elderly.

**Constipation**

*Constipation* is an inability to pass stools. In palliative care patients, prevention is the best therapy. For opioid-induced constipation, recommended agents are stimulant laxatives such as bisacodyl or senna, with or without a stool softener. Other agents such as the osmotic laxatives (e.g., lactulose or polyethylene glycol) may be added to the patient's bowel regimen if needed. Counsel the patient to drink plenty of fluids so the laxative can be effective. A third-line option is methylnaltrexone, an injectable opioid antagonist. It works to inhibit opioid-induced decreased GI motility and delayed GI transit time; it does not cross the blood-brain barrier and, therefore, will not reverse the analgesic effect of the opioids. Other agents may be useful for non-opioid induced constipation (see Chapter 11). Remember that the best way to treat and manage constipation in the palliative care patient is to identify the underlying causes.
### Table 6-4. Selected Agents Used in Hospice and Palliative Care in the Geriatric Population

<table>
<thead>
<tr>
<th>Medication</th>
<th>Use in Palliative Care</th>
<th>Geriatric Starting Dosing (po or transdermal unless otherwise noted)</th>
<th>Special Considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Opioid Analgesics</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fentanyl transdermal</td>
<td>Nociceptive pain</td>
<td>12.5 mcg/hr; titrate based on response</td>
<td>Do not use in opioid-naive patients; absorption may be variable in the elderly</td>
</tr>
<tr>
<td>Hydrocodone/acetaminophen</td>
<td>Nociceptive pain, cough</td>
<td>2.5/325–5/325 mg every 6 hours prn; titrate based on response</td>
<td>MDD of acetaminophen = 3 g</td>
</tr>
<tr>
<td>Hydromorphone</td>
<td>Nociceptive pain</td>
<td>1–2 mg every 4 hours prn; titrate based on response</td>
<td>Not the best first-line opioid for opioid-naive patients</td>
</tr>
<tr>
<td>Methadone</td>
<td>Nociceptive pain</td>
<td>2.5 mg every 12 hr</td>
<td>Do not use in opioid-naive patients</td>
</tr>
<tr>
<td>Methadone</td>
<td>Neuropathic pain</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Morphine extended release</td>
<td>Nociceptive pain</td>
<td>15 mg every 12 hr</td>
<td>Do not crush; active metabolites accumulate in renal insufficiency</td>
</tr>
<tr>
<td>Morphine immediate release</td>
<td>Dyspnea</td>
<td>2.5–5 mg every 1 hr prn</td>
<td>Active metabolites accumulate in renal insufficiency</td>
</tr>
<tr>
<td>Oxycodone extended release</td>
<td>Dyspnea</td>
<td>10 mg every 12 hr</td>
<td>Opioid of choice in the elderly; do not crush</td>
</tr>
<tr>
<td>Oxycodone immediate release</td>
<td>Dyspnea</td>
<td>2.5–5 mg every 1 hr prn</td>
<td>Opioid of choice in the elderly</td>
</tr>
<tr>
<td>Tapentadol</td>
<td>Nociceptive pain</td>
<td>25–50 mg every 6 hr</td>
<td>MDD = 600 mg; adjust dose in hepatic and renal failure; serotonin syndrome can occur if taken with SSRIs/ SNRIs and MAOIs</td>
</tr>
<tr>
<td>Tramadol</td>
<td>Nociceptive pain</td>
<td>25–50 mg every 8 hr</td>
<td>MDD = 600 mg; adjust dose in hepatic and renal failure; serotonin syndrome can occur if taken with SSRIs/ SNRIs and MAOIs</td>
</tr>
<tr>
<td><strong>Non-Opioid Analgesics</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Acetaminophen</td>
<td>Mild to moderate pain</td>
<td>325–650 mg every 6 hr</td>
<td></td>
</tr>
<tr>
<td>Ibuprofen</td>
<td>Bone pain</td>
<td>400 mg every 8 hr</td>
<td>MDD = 3200 mg; give with PPI to prevent GI problems</td>
</tr>
<tr>
<td>Meloxicam</td>
<td>Bone pain</td>
<td>7.5 mg daily</td>
<td>MDD = 15 mg, less GI side effects than other NSAIDs</td>
</tr>
<tr>
<td></td>
<td>Inflammatory nociceptive pain</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
### Naproxen
- **Bone pain**
- **Inflammatory nociceptive pain**
- **DOSAGE**: 250 mg every 12 hr
- **MDD = 1500 mg; give with PPI to prevent GI problems**

### Adjuvant Analgesics

<table>
<thead>
<tr>
<th>Drug</th>
<th>Pain Type</th>
<th>Dosage</th>
<th>MDD Limitation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Desipramine</td>
<td>Neuropathic pain</td>
<td>10–25 mg at bedtime</td>
<td>Less anticholinergic side effects when compared to amitriptyline and doxepin</td>
</tr>
<tr>
<td>Duloxetine</td>
<td>Neuropathic pain</td>
<td>20 mg daily</td>
<td>MDD = 60 mg; not recommended in hepatic failure or if CrCl &lt; 30 mL/min</td>
</tr>
<tr>
<td>Gabapentin</td>
<td>Neuropathic pain</td>
<td>100 mg twice daily</td>
<td>MDD = 3600 mg; often better tolerated than pregabalin, adjust dose in renal insufficiency</td>
</tr>
<tr>
<td>Lidocaine patch</td>
<td>Neuropathic pain</td>
<td>On 12 hr, off 12 hr</td>
<td>MDD = 3 patches per 12 of 24 hr; few side effects; caution in liver failure (reduced clearance)</td>
</tr>
<tr>
<td>Nortriptyline</td>
<td>Neuropathic pain</td>
<td>10–25 mg at bedtime</td>
<td>Tricyclic antidepressant of choice in the elderly; less anticholinergic effect when compared with amitriptyline or doxepin</td>
</tr>
<tr>
<td>Pregabalin</td>
<td>Neuropathic pain</td>
<td>25 mg three times per day</td>
<td>MDD = 600 mg (doses greater than 300 mg/day may offer no additional benefit); adjust dose based on CrCl</td>
</tr>
<tr>
<td>Venlafaxine</td>
<td>Neuropathic pain</td>
<td>25–50 mg twice daily (immediate release) or 37.5 mg once daily (extended release)</td>
<td>MDD = 225 mg; reduce dose in renal and hepatic failure</td>
</tr>
</tbody>
</table>

### Bisphosphonates

<table>
<thead>
<tr>
<th>Drug</th>
<th>Pain Type</th>
<th>Dosage</th>
<th>MDD Limitation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Zoledronic acid</td>
<td>Bone pain and prevention of skeleton-related events (e.g., fractures)</td>
<td>4 mg IV once every 3–4 weeks</td>
<td>Adjust dose when CrCl &lt; 60 mL/min; do not use when CrCl &lt; 30 mL/min</td>
</tr>
<tr>
<td>Pamidronate</td>
<td>Bone pain and prevention of skeletal-related events (e.g., fractures)</td>
<td>90 mg IV over 2.5 hr once every 3–4 weeks</td>
<td>Use not recommended with severe renal impairment</td>
</tr>
<tr>
<td><strong>Bone-Modifying Agents</strong></td>
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<tr>
<td><strong>Denosumab</strong></td>
<td>Bone pain and prevention of skeletal-related events (e.g., fractures)</td>
<td>120 mg SC every 4 weeks</td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th><strong>Corticosteroids</strong></th>
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<tbody>
<tr>
<td><strong>Dexamethasone</strong></td>
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<tr>
<th><strong>Antipsychotic Agents</strong></th>
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<tbody>
<tr>
<td><strong>Chlorpromazine</strong></td>
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<td></td>
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<tr>
<td><strong>Haloperidol</strong></td>
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<table>
<thead>
<tr>
<th><strong>Benzodiazepines</strong></th>
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</thead>
<tbody>
<tr>
<td><strong>Lorazepam</strong></td>
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<td></td>
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<tr>
<td><strong>Midazolam</strong></td>
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<tr>
<td></td>
</tr>
<tr>
<td><strong>Oxazepam</strong></td>
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<table>
<thead>
<tr>
<th><strong>Antidepressants</strong></th>
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</thead>
<tbody>
<tr>
<td><strong>Citalopram</strong></td>
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<tr>
<td><strong>Mirtazapine</strong></td>
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<td></td>
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<tr>
<td><strong>Sertraline</strong></td>
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</tbody>
</table>
### Psychostimulants

<table>
<thead>
<tr>
<th>Drug</th>
<th>Indications</th>
<th>Dosage</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Methylphenidate</td>
<td>Depression in terminally ill patients, Fatigue in advanced disease</td>
<td>2.5 mg in the morning</td>
<td>MDD = 20 mg; if twice-daily dosing, 2nd dose should not be later than noon</td>
</tr>
</tbody>
</table>

### Miscellaneous Antianxiety Agents

- **Buspirone**  
  **Indications**: Anxiety  
  **Dosage**: 7.5 mg twice daily

### Appetite Stimulants and Agents Used for Appetite

<table>
<thead>
<tr>
<th>Drug</th>
<th>Indications</th>
<th>Dosage</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Megestrol acetate</td>
<td>Anorexia</td>
<td>160 mg/day</td>
<td>MDD = 800 mg</td>
</tr>
<tr>
<td>Dronabinol</td>
<td>Anorexia</td>
<td>2.5 mg twice daily</td>
<td>MDD = 20 mg</td>
</tr>
<tr>
<td>Metoclopramide</td>
<td>Anorexia, Gastric stasis–induced nausea and vomiting</td>
<td>5 mg twice daily</td>
<td>MDD = 80 mg</td>
</tr>
</tbody>
</table>

### Anticholinergic Agents

<table>
<thead>
<tr>
<th>Drug</th>
<th>Indications</th>
<th>Dosage</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Atropine</td>
<td>Terminal secretions</td>
<td>0.4–0.6 mg every 4 hr prn</td>
<td>Ophthalmic solution may be administered sublingually; anticholinergic side effects, especially in the elderly (delirium, lethargy, urinary retention, constipation)</td>
</tr>
<tr>
<td>Hyoscyamine</td>
<td>Terminal secretions</td>
<td>0.125 mg every 6 hr prn</td>
<td>MDD = 1.5 mg; same side effects as above</td>
</tr>
<tr>
<td>Glycopyrrolate</td>
<td>Terminal secretions</td>
<td>0.2–0.4 mg to 2 mg IV or SC every 4 hr prn</td>
<td>Same side effects as above; may be better tolerated</td>
</tr>
</tbody>
</table>

MDD, maximum daily dose; MAOI, monoamine oxidase inhibitor; po, by mouth; PPI, proton pump inhibitor; prn, as needed; GI, gastrointestinal; NSAID, nonsteroidal anti-inflammatory drug; CrCl, creatinine clearance; IV, intravenous; SC, subcutaneous; SNRI, selective serotonin/norepinephrine reuptake inhibitor; SSRI, selective serotonin reuptake inhibitor.

For additional information, see references 16 and 38.

### Pruritus

Pruritus (itching) is not a common symptom in palliative care, but when it occurs it can be very bothersome for the patient. Severe itching seen in patients with advanced disease is usually associated with uremia, cholestasis, opioids, solid tumors, and hematologic disorders. Previously, H₁ receptor antagonists were the drug of choice for pruritus. However, in the palliative care setting, pruritus is not usually due to histamine release and, therefore, antihistamines are not typically beneficial. Serotonin may have a role in pruritus secondary to malignant disease, uremia, and opioids. Therefore, selective serotonin reuptake inhibitors (SSRIs) may be reasonable medications to try in these patients. It is better to start with small doses; effects are usually seen within 24–48 hours. Another agent with similar benefits is mirtazapine 15 mg at bedtime. Ondansetron, a 5-HT₃ receptor antagonist, may be tried; however, it is more expensive and may cause constipation.

### Anxiety and Depression

Depression is common among older adults with advanced illness; however, it is often under-recognized and undertreated. Diagnosing...
depression is difficult in elderly patients who are in the final stages of life, especially if they also have cognitive dysfunction.\textsuperscript{58,59} Treatment of depression in a palliative care patient is dependent on the severity of the depression, the patient’s ability to respond to nonpharmacological therapy (e.g., psychotherapy), and life expectancy. First-line pharmacologic treatment of depression in the elderly is usually initiated with SSRIs, such as sertraline, citalopram, and escitalopram. These are well tolerated, have few drug-drug interactions, and have a low side effect profile.\textsuperscript{38} Another agent that may be beneficial is mirtazapine; lower doses are more sedating, if insomnia is a problem. Taking advantage of the side effect profile of a medication can help treat bothersome symptoms associated with the end of life. The TCAs as well as the SNRIs may be useful and should be considered in patients who experience chronic pain or neuropathic pain syndromes.\textsuperscript{60}

All of these agents take 4–6 weeks to show an antidepressant effect. Unfortunately, if a patient has <2 months to live, this would not allow enough time for a benefit to be seen. Psycho-stimulants (e.g., methylphenidate, dextroamphetamine) are beneficial in providing a rapid response in mood elevation in certain situations as described above. However, signs and symptoms of agitation must be monitored, because this is a potential side effect.\textsuperscript{58} Overstimulation, another side effect, is rarely a concern because terminally ill patients usually experience fatigue.\textsuperscript{38}

Anxiety is the most common mental disorder and is prevalent at the end of life.\textsuperscript{61} Early stages of delirium may mimic anxiety, and undertreated pain and dyspnea can cause or worsen anxiety. The drugs discussed above are generally preferable in palliative care, because the older antipsychotics or antiemetics have side effects that mimic anxiety (e.g., akathisia).\textsuperscript{38} Untreated anxiety may hinder the ability to achieve treatment goals.

Nonpharmacologic management of anxiety should be addressed, including identification and treatment of the underlying cause (when possible) as well as emotional support. Some patients exhibit signs and symptoms of pathologic anxiety (see Table 6-5). Usually, this type of anxiety must be managed with SSRIs and buspirone, the agents of choice for general anxiety disorder in the elderly. These drugs, however, are only advantageous if the patient has a 2-month or longer life expectancy.\textsuperscript{62,63} For acute anxiety, benzodiazepines are best. If the patient also has delirium, other agents such as typical and atypical antipsychotics may be used. Benzodiazepines have an increased risk of causing falls and cognitive impairment. Lorazepam and oxazepam are the preferred agents because they have no active metabolites and intermediate half-lives. If benzodiazepines worsen or cause delirium, low-dose risperidone or haloperidol may be used.\textsuperscript{38}

<table>
<thead>
<tr>
<th>Table 6-5. Behaviors Associated with Pathologic Anxiety</th>
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<tbody>
<tr>
<td><strong>Intense worry or dread</strong></td>
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<tr>
<td><strong>Physical distress (e.g., tension, restlessness)</strong></td>
</tr>
<tr>
<td><strong>Maladaptive behaviors (e.g., treatment nonadherence, social withdrawal, avoidance)</strong></td>
</tr>
<tr>
<td><strong>Diminished coping</strong></td>
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<tr>
<td><strong>Inability to relax</strong></td>
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<tr>
<td><strong>Depression</strong></td>
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<tr>
<td><strong>Fatigue</strong></td>
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<tr>
<td><strong>GI upset</strong></td>
</tr>
<tr>
<td><strong>Dyspnea</strong></td>
</tr>
<tr>
<td><strong>Dysphagia</strong></td>
</tr>
</tbody>
</table>

For additional information, see reference 38.

**Nausea and Vomiting**

Up to 70% of palliative care patients experience nausea and vomiting, often in the last 6 weeks of life.\textsuperscript{64} Uncontrolled nausea and vomiting are extremely distressing and decrease a patient’s quality of life. There are many causes, and the specific origin of a patient’s symptoms should be identified to best treat or prevent them. Some causes of nausea and vomiting are constipation, medications, infection, bowel obstruction, increased intracranial pressure, chemotherapy, and untreated pain.\textsuperscript{55} Nonpharmacologic therapies are discussed in Chapter 11.
Four main mechanisms of nausea and vomiting are stimulation of the chemoreceptor trigger zone, pathology of the cerebral cortex, GI dysfunction, and vestibular activity. Pharmacologic treatment aims to block stimulation of at least one of these mechanisms. Table 6-6 lists common causes and possible medications to treat different types of nausea in palliative care. In terminally ill patients, stimulation of the chemoreceptor trigger zone is the most common cause. The most common neurotransmitters involved are dopamine (D2), serotonin, and neurokinin-1. Treatment is usually based on blocking the actions of D2 at the D2 receptor. Initiate treatment with low doses in the elderly to decrease the chance of unwanted side effects. Chapter 11 discusses these agents in detail.

Other potential causes include gastritis, gastroesophageal reflux disease, and peptic ulcer disease. These should be treated with histamine antagonists or proton pump inhibitors.64-67 Medications used to treat refractory nausea and vomiting include combinations of agents listed in Table 6-6 as well as agents mentioned in Chapter 11.38

**KEY POINT:** In treating nausea, remember (1) prevention is the best treatment, (2) treatment via oral routes is as effective as parenteral routes, (3) initiate with the lowest effective dose, and (4) when selecting an agent, consider the side effects.

Although many agents treat and prevent nausea, no current standard exists for antiemetic therapy in the elderly, so that evidence comparing the different agents in this patient population is limited.56

**Anorexia**

Anorexia is a loss of appetite resulting in decreased intake. It is a common GI disorder that may occur in patients with advanced illness. It can be bothersome not only for patients but also family members. The disorder can occur alone, or in combination with many end-of-life diseases, such as cancer, acquired immune deficiency syndrome (AIDS), COPD, dementia, and heart failure. Before initiating pharmacologic treatment, reversible and underlying causes should be ruled out.68 These include (but are not limited to) pain, mucositis, delirium, GI causes (e.g., constipation, nausea and vomiting, delayed gastric emptying), depression, and endocrine disorders (e.g., thyroid dysfunction, metabolic abnormalities). Once these causes are addressed, pharmacologic considerations may be considered. These interventions will likely have no impact on survival; therefore, treatment is usually aimed at improving quality of life by decreasing symptoms, which include lack of appetite, nausea, early satiety, and fatigue.69 However, it is important to note that when death is imminent, patients are normally not hungry. Fluids and food should never be forced on the patient, for even the presence of food in the stomach may produce pain.

If treatment is warranted, it should be aimed at providing pharmacologic as well as nonpharmacologic options. Nonpharmacologic approaches include dietary alterations, such as eating several small meals throughout the day instead of three large meals, and advising the patient to eat his or her favorite meals while getting rid of meals with strong tastes or odors.68 The dying patient is also likely to experience dysgeusia, a condition in which the sense of taste may be radically altered, causing foods and beverages once pleasant to be perceived as repellent. Helpful approaches will vary from patient to patient.

Medications used to stimulate appetite may offer symptomatic relief. Some of the most common agents used to stimulate appetite are listed in Table 6-4. Megestrol acetate and corticosteroids have the most evidence of efficacy in anorexia. Other agents have been used, but with limited evidence for improvement of appetite or weight.68 Megestrol acetate is the most studied agent, although it is recommended for use with caution in elderly patients. Starting doses of 160 mg/day have shown improvements in not
only appetite but fatigue and overall quality of life as well. Although doses up to 800 mg/day have been shown to be optimal for treatment of anorexia in patients with cancer, there are dose-related side effects and increased costs at higher doses. Therefore, start at lower doses and increase as clinically needed and tolerated. The mechanism of action of megestrol acetate is not completely understood; however, it is thought to be related in part to glucocorticoid activity.

Corticosteroids are another class of medications that have shown temporary benefit (over several weeks) in appetite in many randomized controlled trials versus placebo. Corticosteroids have also shown improvements in pain (as mentioned above), nausea, and well-being; however, none of these studies have actually shown improvements in weight. Due to the risk of side effects with prolonged use, these agents should be saved for patients with a life expectancy of <6 weeks, and those with other symptoms, such as nausea or pain. At present, no studies have shown the best dosing regimen and schedule; however, it is considered appropriate in the geriatric population to start with low doses given earlier in the day to avoid side effects such as insomnia.

Table 6-6. Pharmacologic Therapy Used for Nausea and Vomiting

<table>
<thead>
<tr>
<th>Cause of Nausea and Vomiting</th>
<th>Examples</th>
<th>Pharmacologic Therapy</th>
</tr>
</thead>
</table>
| Chemoreceptor trigger zone induced | 1. Opioids  
2. Chemotherapy  
3. Bacterial toxins  
4. Uremia | 1. Butyrophenones (e.g., haloperidol)  
2. Phenothiazines (e.g., prochlorperazine)  
3. Metoclopramide  
4. Serotonin antagonists (e.g., ondansetron, granisetron) |
| GL tract induced | 1. Gastric stasis  
2. Gl obstruction  
3. Drugs and diseases that decrease gastric emptying (e.g., opioids and occurs with diabetes mellitus, chronic renal failure, and neurological disorders)  
4. Metastatic disease  
5. Bacterial toxins  
6. Chemotherapy  
7. Radiation therapy | 1. Metoclopramide  
2. Anticholinergics (e.g., hyoscyamine) |
| Cerebral cortex induced | 1. Anticipatory (anxiety, taste, or smell induced)  
2. Intracranial pressure induced | 1. Anticipatory-induced nausea and vomiting is usually treated with anxiolytics, such as benzodiazepines (e.g., lorazepam, alprazolam)  
2. Intracranial pressure-induced nausea and vomiting may be treated with corticosteroids (e.g., dexamethasone) |
| Vestibular activity induced | 1. Opioids  
2. Movement induced | 1. Antihistamines (e.g., meclizine)  
2. Anticholinergics (e.g., scopolamine) |

These medications are used mainly for chemotherapy- and radiotherapy-induced nausea. Dexamethasone may be used for nonspecific nausea and vomiting; the mechanism of action is unknown. Use with caution in the elderly; may cause confusion, constipation, urinary retention, and orthostatic hypotension. For additional information, see reference 38.
Cannabinoids are well known for their ability to increase appetite. Dronabinol and nabilone are synthetic agents in this class. Using these agents to stimulate appetite in diseases other than AIDS-related cachexia is considered an off-label use. Studies evaluating dronabinol at doses of 2.5–5 mg twice to three times daily have shown significant improvements in appetite in patients with AIDS and cancer-related cachexia. However, as with other agents, there was little to no improvement in weight. Another study evaluating dronabinol versus megestrol acetate for advanced cancer showed megestrol acetate to be more beneficial for improving appetite. These agents may also improve mood and decrease nausea, but their use is often limited due to central nervous system side effects. In elderly patients, these side effects may be exaggerated due to increased sensitivity to medications and other medications the patient may take that affect the central nervous system. It is important to remember to titrate the dose slowly based on clinical response.

Metoclopramide is sometimes recommended for treatment of anorexia; however, it is usually reserved for patients with symptoms of delayed gastric emptying that can lead to nausea and early satiety. It has little effect on appetite. Metoclopramide has prokinetic properties and increases motility through the GI tract. By decreasing nausea and early satiety, it may indirectly lead to increased appetite. Metoclopramide requires dosing four times per day and can have severe side effects. Dosing for elderly patients should be at the lower end of the recommended range and adjusted for renal function.

Mirtazapine is known to cause weight gain and increased appetite in patients treated for depression. Because of this effect, it has been used for appetite stimulation in patients with advanced diseases. It can also cause sedation, which may be helpful for patients suffering from insomnia. Mirtazapine clearance is decreased by 40% in elderly males and 10% in elderly females; therefore, starting at a lower dose is best. Optimal dosing regimens are not well defined due to lack of controlled trials. However, it is important to remember to start at lower doses and increase based on clinical effect and tolerance.

Fatigue

Fatigue is common in advanced disease. There are many studies evaluating assessment tools for fatigue in patients with advanced disease, but few of them have been validated in geriatric patients. There are limited data available about the best treatment for fatigue.

Stimulants (e.g., methylphenidate) are often prescribed, but at present there are no studies with definitive guidance or support for this. A literature review of 19 controlled trials evaluated methylphenidate in palliative care patients or older patients with advanced disease. This review showed conflicting results, had a small sample size, and the authors were unable to conclude whether this medication was effective. Another study found that overall, methylphenidate was not effective in treating cancer-related fatigue; however, in the patients with more advanced disease or more severe fatigue, the study found that the patients receiving methylphenidate did better overall. Although stimulants are used, more studies are needed to assess their use in palliative care.

Dyspnea

Dyspnea, described as shortness of breath, chest tightness, inability to get enough air, and a feeling of drowning or suffocation, tends to worsen in the last weeks of life. These symptoms are more common in older patients and produce a decreased quality of life. Symptoms may be worsened or caused by medication side effects (e.g., chemotherapy), decreases in muscle mass in older adults, pulmonary edema associated with heart failure, anemia as seen with end-stage kidney disease, infection, depression, bronchospasm, and anxiety. Dyspnea is subjective, and patient self-report is the only dependable marker. Nonpharmacologic treatment may be helpful, such as identifying and avoiding triggers that can cause attacks (e.g., strong perfumes, smoking), using fans or open windows to improve air circulation, correct posi-
tioning to provide comfort (especially in patients with COPD), and relaxation exercises that may decrease anxiety. In the pharmacologic management of dyspnea, many studies show improvement with the use of opioids. Opioids are often considered first-line therapy in end-of-life care, once other causes are ruled out, or if treatment of other causes does not completely ease the dyspnea. In dyspnea, the main mechanism of action of opioids is the reduction of the response to hypoxia and hypercapnia, thereby decreasing the patient’s awareness of the breathing state. Doses used are much smaller than those for pain treatment and may be given every 1–2 hours as needed. A long-acting opioid may be initiated for patients requiring frequent administration to control their symptoms.

Benefit has been shown with both oral and parenteral opioid dosing, but it is unclear whether using nebulized opioids is of any benefit. Regardless, many patients and physicians report decreased dyspnea symptoms with nebulized opioids. Advantages are fast action and possibly fewer side effects (due to decreased bioavailability). Several uncontrolled trials have shown benefit with nebulized morphine at doses of 10–40 mg. Studies have shown that although dyspnea symptoms decrease with opioid use, respiratory rate does not change, indicating safety with opioid use.

Other options for treatment of dyspnea are benzodiazepines and use of oxygen. Benzodiazepines may help with feelings of anxiety associated with breathlessness. In the elderly, low doses of benzodiazepines, such as lorazepam 0.25 mg every 6–8 hours as needed, should be used. Studies evaluating the use of oxygen for management of dyspnea suggest that for patients without hypoxia, using oxygen for dyspnea is no better than breathing room air.

Other treatment options for dyspnea depend on the underlying cause. For example, in patients with advanced heart failure, diuretics are the mainstay of treatment. Eventually, these patients may develop diuretic resistance and require other pharmacologic treatment, such as isosorbide dinitrate, hydralazine, and inotropic agents (e.g., milrinone, dobutamine). For patients suffering from end-stage COPD, bronchodilators (e.g., albuterol, ipratropium) or oral steroids for inflammation may be considered. Nebulized bronchodilators may be more effective in patients who cannot use inhalers because they are weak and have a difficult time actuating the inhaler. It may also be useful to consider adding a cough suppressant such as dextromethorphan or hydrocodone in patients who have dyspnea from extreme coughing.

**KEY POINT:** Studies have shown that although dyspnea decreases with opioid use, respiratory rate does not change, indicating safety with opioid use.

### Agitation and Delirium

Agitation, hallucinations, and delirium are associated with cognitive impairment and result in patient and family distress. Delirium is one of the most common reasons to use palliative sedation, discussed below. Reversible causes of delirium or agitation such as infection, untreated pain, dehydration, metabolic disturbances, side effects of drugs, urinary retention, constipation or fecal impaction, and alcohol or drug withdrawal should be identified and treated. Once delirium is identified with no reversible causes, there are mixed recommendations as to the best management.

Delirium occurs in >80% of terminally ill patients, usually during the last few days of life. Patients with delirium may demonstrate confusion or an inability to either continue or alter attention. Sundowning is a common phenomenon in terminally ill, end-of-life patients, particularly those suffering from delirium, characterized by daytime sleepiness and nighttime agitation or inability to rest. Patients may demonstrate hypoactive delirium or delirium with agitation; either way, treatment is still the same.
logical treatment may only be necessary if the patient is aggressive or agitated. Those who are not agitated may only require comfort.

Antipsychotics (conventional or atypical) are the most common agents used for treatment of agitation. Use of these medications for treatment of delirium is an off-label use. In palliative care, haloperidol is the drug of choice. Doses <2 mg/day are usually well tolerated and nonsedating. In some cases, the goal of therapy is sedation; for example, patients with terminal delirium who are agitated or aggressive, with whom chlorpromazine may be used, because it provides more sedation than haloperidol.100-103 Although chlorpromazine can cause orthostatic hypotension, this is not a concern when patients are confined to a bed and at the end of life. If patients are unable to swallow, both of these medications may be given sublingually or rectally, although these are not approved dosage routes. Haloperidol can also be given subcutaneously104 at 50% of the oral dose.35

Atypical antipsychotics (e.g., quetiapine, risperidone, olanzapine) may be used to manage delirium. Risperidone is available in a rapidly dissolving oral dosage form for those unable to swallow. Olanzapine is commercially available for intramuscular injection. These alternative dosage forms may be beneficial in certain situations. Benzodiazepines given alone for treatment of delirium may worsen the delirium and confusion. Occasionally, it is beneficial to add benzodiazepines to antipsychotics if sedation is necessary.105

Terminal Secretions

Terminal secretions, also known as the death rattle, occur when the patient has only days or hours left to live. Studies show that terminal secretions are predictive of impending death, with up to 76% dying within 48 hours of onset.106 Patients lose the ability to swallow their oral secretions, which accumulate in the airway and as air passes through the mucus cause a rattling or gurgling sound.106 This is disconcerting to the patient’s family present at the bedside. Treatment is usually indicated due to the distressing impact on the family. Sometimes, elevating the head of the bed and positioning the patient somewhat on one side may help the secretions drain out of the airways. Symptoms should also lessen as the patient becomes more dehydrated. If there is no improvement, or if the symptoms cause extreme anxiety among family, anticholinergic agents may be used.106-109 These medications help to further reduce secretions. They do not decrease existing secretions and, therefore, work best when given at symptom onset. Anticholinergics that may be used include atropine, hyoscyamine, and glycopyrrolate. Doses for the elderly should be given at the lower end of those prescribed in younger adults. These medications should not be used in those who experience secretions secondary to pneumonia or pulmonary edema.109

Proportionate Palliative Sedation

Sometimes, it may be difficult to control intractable physical symptoms in actively dying patients. In these circumstances, intractable symptoms at the end of life may be managed by using increasingly higher levels of sedation, known as proportionate palliative sedation.110-112 The goal of this type of treatment is to ease unmanageable suffering in patients who are imminently dying (i.e., days to 1–2 weeks left). The purpose is not to end a patient’s life or to speed up death. Situations in which proportionate palliative sedation may be considered in an actively dying patient after other treatments have failed are intractable nausea and vomiting, unmanageable pain, agitated terminal delirium, and unrelenting dyspnea.16 This type of treatment is intended to attain the least amount of sedation needed in order to control the patient’s symptoms. Treatment of the patient’s other symptoms should be continued as well, in addition to the sedation.

Proportionate palliative sedation is different from palliative sedation to unconsciousness. The latter is a controversial type of management in which the end goal is unconsciousness to relieve unmanageable symptoms. Proportionate palliative sedation is intended only to sedate the patient enough to control the symptoms. Some-
times, unconsciousness is unavoidable, but that is not the goal. Ordinary sedation is another management strategy that should be distinguished from proportionate palliative sedation. In this type of practice, sedatives are used to aid in sleep or to help treat anxiety symptoms, but consciousness is preserved.\textsuperscript{110}

It is important to follow appropriate guidelines when initiating proportionate palliative sedation, such as transferring the patient to an individual room, allowing family unlimited visiting rights (according to the patient's wishes), measuring and documenting baseline assessment of symptoms, and continuing other successful symptom management along with the sedation. The healthcare team should initiate treatment and assess symptoms according to a formal protocol, including having the physician present when the infusion is initiated and remaining available until unrelieved symptoms are stabilized, monitoring to determine the patient's level of sedation needed to control the unrelenting symptoms, and having a provision to increase the dose if the symptoms are unrelieved over a mutually agreed-on time frame. A dose increase is accomplished by administering an additional bolus dose and then increasing the infusion rate by 20\% to 30\%.

The most common agent used for palliative sedation is midazolam. Other agents used are lorazepam and phenobarbital.\textsuperscript{112} The infusion should be maintained at a rate that is adequate to control the symptoms. If proportionate palliative sedation is chosen as an option for symptom management for the dying patient, it is important to provide family support, with updates and attention to their emotional needs and grief.\textsuperscript{112}

\section*{Grief When Death Occurs}

After a loved one dies, family and friends go through a process of grief. There are different types of grief. Prior to death, the patient and family may experience what is known as anticipatory grief. The patient may think about his or her life and consider what he or she might have changed, as well as express feelings of love, gratitude, and forgiveness.\textsuperscript{113}

Grief occurs after the patient dies and includes a wide spectrum of feelings and experiences.\textsuperscript{114} Family members may experience disbelief, longing, anger, and acceptance in no particular order. Although family and friends will never completely forget their sense of loss, this feeling should lessen over time. A severe sense of loss and grieving that lasts more than 6 months may indicate complicated grief. This type of grief usually affects a person's work or social life.\textsuperscript{116}

There are tools that may be implemented and used for guidance when responding to grief. One tool is called the EASE Tool. This tool stands for Educate family and friends about how their feelings accompanying normal grief are acceptable; Assess common grief reactions; Support the family by listening; and Explore with them what methods may help them best while they are grieving.\textsuperscript{115}
**CASE 1: PALLIATIVE CARE CONSULT**

**Setting:**
Hospital.

**Subjective:**
CF is a 76-year-old African American woman admitted to the hospital 3 days ago from the geriatric clinic, where she has been followed for several years. Her chief complaint at hospital admission was altered mental status, reported by her daughter, who accompanied her to clinic. Beginning 3 months ago she developed right-sided facial palsy and blurry vision. Head CT scan at that time was negative. She subsequently developed urinary incontinence and gait disturbance with impaired coordination and imbalance. Over the past 10 days, she stopped eating and became confused. In the hospital she was treated with aggressive hydration for acute kidney injury, ceftriaxone for a urinary tract infection, and an enema for constipation. She had no advanced directives and was full code at this time. Further workup revealed a lung mass on chest CT scan and two metastatic lesions on her brain MRI. Palliative care was consulted for recommendations with pain/symptom management and discussion of goals of care. The palliative care team, consisting of a physician, advanced practice nurse, pharmacist, and chaplain met the patient at bedside with family present.

**Past Medical History:**
Hypertension, diabetes, lung cancer S/P resection 19 years ago.

**Medications:**
Prior to admission CF was taking amlodipine 10 mg daily, meloxicam 7.5 mg daily, metformin 500 mg twice daily, carboxymethylcellulose eye drops to right eye. At present she is on a normal saline infusion 100 mL/hr, ceftriaxone 1 g IVPB daily, heparin 5,000 units q 8 hours, sliding scale regular insulin, vitamin D 1000 units daily, carboxymethylcellulose eye drops to the right eye as needed, and milk of magnesia 30 mL daily.

**Social History:**
Widowed x10 years with six children and five grandchildren. Currently lives with sister in rural part of the state. Current smoker of ½ pack for 60 years. No alcohol or illicit drugs. She is Baptist, and her religion/spirituality are very important to her.

**Review of Systems:**
Positive for weight loss, concentration difficulties, disorientation, and memory problems; also positive for not able to close right eye, constipation, gait disturbance, and urinary incontinence.

**Objective:**
Wt 53.4 kg, Ht 66˝, BP 150/90 mmHg, P 90 BPM, T 98°F, RR 18/min

**Physical Examination:**
Pleasant cachectic elderly woman lying in bed in no acute distress. Dry mucus membranes and skin. Facial droop on the right. Positive screen for delirium (acute onset, fluctuating, inattentive). The rest of the physical exam was noncontributory.

**Labs:**
Sodium 143 mEq/mL, potassium 4.6 mEq/mL, chloride 106 mEq/mL, calcium 10.5 mEq/mL, BUN 42 mEq/mL, serum creatinine 1.6 mEq/mL, glucose 120 mg/dL, WBC 9.45, Hgb 15.3, Hct 44.5%, platelets 618, vitamin D 20.6 ng/mL.
Assessment:
Patient with dehydration and UTI on admission which are now resolved and altered mental status improved. Palliative care consulted for review of goals of care, given new diagnosis of recurrent lung cancer with brain metastases. Patient is also experiencing delirium, constipation, and lack of oral intake.

Plan:
1. Discussed goals of care and hospice with family and patient, noting patient was delirious. Patient agreed that family could make decisions for her. Her children are in agreement that she would not wish for aggressive treatment and would agree to Do Not Resuscitate status based on previous conversations with her. Patient will be transferred to an inpatient hospice or nursing home with hospice now that she is stable.
2. Begin dexamethasone 2 mg IV daily and nicotine transdermal patch 21 mg daily.
3. Discontinue sliding scale insulin and vitamin D, and do not re-initiate metformin or amlo-dipine at discharge. Continue home medication of meloxicam at discharge.
4. Begin morphine sulfate 1–2 mg IV every 1–2 hours as needed for pain or agitation. Replace milk of magnesia with senna 8.6 mg daily.
5. Contact minister of local church for spiritual support after discharge.

Rationale:
1. For African American patients, family and close friends are often an important source of support for making healthcare decisions surrounding the end of life. Involving the family is an important step in identifying the patient’s wishes for most people from this culture. The palliative care team can be instrumental in explaining issues and involving appropriate individuals to ascertain the patient’s wishes. The experience with death and dying and the interprofessional composition of the team are key to achieving good outcomes in this setting.
2. The patient’s symptoms of palsy, gait disturbance, and delirium may be due to the metastatic lesions or may be secondary to either associated brain edema or (for delirium) withdrawal from cigarette smoking. Beginning dexamethasone and nicotine may address the symptoms to improve quality of life over the next few weeks.
3. Treatment of hypertension and diabetes mellitus to prevent long-term morbidity and mortality is no longer a priority given the estimated life expectancy. Similarly, treating vitamin D deficiency is unlikely to affect any of CF’s current complaints. Reducing pill burden is a goal at this time.
4. Most hospice patients have pain complaints or agitation resulting from pain. Meloxicam may be continued as a component of pain management, but having low, frequent doses of morphine sulfate available on an as-needed basis for an opioid-naive patient is appropriate for breakthrough pain and an expected escalation of pain that will occur as the disease progresses. An appropriate bowel regimen would include a motility agent such as senna or bisacodyl.
5. Including spiritual advisors familiar to the patient and family at the end of life provides continuity and support.

Case Summary:
This case provides an example of palliative care providers working with a patient and family to revise goals of care and identify hospice as an alternative to dying in the hospital. Review of medications for appropriateness given the new goals of care with a focus on symptom management rather than long-term prevention of morbidity and mortality is a role for pharmacists involved in palliative care. Offering support adapted to a patient’s cultural beliefs and spiritual needs completes the holistic approach required for the best outcomes.
**Case 2: Hospice Care**

**Setting:**
Recently discharged from hospital admission to home hospice care.

**Subjective:**
AK is a 76-year-old man who presents to home hospice with worsening pain in his bones due to metastatic prostate cancer. He was recently discharged from the hospital. On this admission his pain regimen was increased. He reports taking his morphine immediate-release tablets every 4 hours around the clock, but they do not control his pain. He also reports fatigue throughout the day that is bothersome because he wants to spend as much time as he can with his family, although he reports it is difficult to sleep at night. AK also reports a decrease in appetite over the last month. Since deciding to transition to hospice, he has noticed more anxiety and depressed days.

**Past Medical History:**
Metastatic prostate cancer (initially diagnosed 8 years ago; metastatic disease to the bone, liver, and lung), hypercholesterolemia, neuropathic pain, depression.

**Medications:**
Oxycodone immediate release 10 mg every 4 hours as needed for pain, oxycodone extended release 30 mg every 12 hours, simvastatin 20 mg daily, gabapentin 600 mg twice daily, duloxetine 20 mg once daily.

**Allergies:**
None.

**Social History:**
Retired professor from community college; lives with wife; has children who are all very close to their parents; attended a Methodist church until recently, when his pain worsened.

**Family History:**
Noncontributory.

**Objective:**
Ht 70”, Wt 159 lb, BP 135/83 mmHg, P 83 BPM, RR 17/min.

**Physical Examination:**
Recent CT scan showing worsening disease in L4 and L5 regions of the spine, new lesions present in liver, increase in size of lesions in lung compared to previous scan, increased pain in spine.

**Labs:**
CBC within normal limits except hemoglobin 10.2 g/dL, hematocrit 32.6%, electrolytes within normal limits, BUN 17 mg/dL, serum creatinine 1.1 mg/dL.

**Assessment:**
AK is a 76-year-old man with worsening metastatic prostate cancer recently enrolled in home hospice for management of symptoms and comfort care. It is estimated that AK has a prognosis of <6 months to live, and likely <2 months.
Plan:
1. Increase oxycodone extended release to achieve better pain control. Counsel patient that he can take oxycodone immediate release every 1–2 hours as needed instead of every 4 hours. Add meloxicam 7.5 mg for treatment of bone pain.
2. Add methylphenidate 2.5 mg in the morning to decrease disease-associated fatigue as this is distressing to the patient.
3. Add mirtazapine 7.5 mg at bedtime to help with sleep and appetite.
4. Consider increasing duloxetine dose; however, based on patient’s limited life expectancy of <2 months, this may not be beneficial.
5. Discontinue simvastatin because it is not improving AK’s quality of life and only adding to his pill burden.
6. Offer to invite a chaplain or his home pastor to visit with him and his family.

Rationale:
1. Currently, AK is taking his immediate-release breakthrough medication every 4 hours around the clock with no relief. In this case, his extended-release pain medication should be increased. It is also advisable to instruct the patient to take his immediate-release oxycodone every 1–2 hours as needed instead of every 4 hours. This allows the patient to take the medication based on the peak effect rather than the duration of action (i.e., 4 hours). It would also be beneficial to the patient to add meloxicam to his medication list. NSAIDs have been shown to decrease bone pain in patients with bone metastases. Starting at a lower dose would be appropriate in an elderly patient. Meloxicam is given once daily and has fewer GI side effects than some of the other NSAIDs, and this is why it was chosen.
2. AK complains of fatigue during the day that interferes with time with his family. In this case, methylphenidate would be an appropriate option to offer this patient. This medication may help decrease the fatigue. In addition, psychostimulants can provide a rapid response in mood. In this patient with worsening depression and a life expectancy of <2 months, methylphenidate may help with these symptoms.
3. Another complaint that is affecting AK’s quality of life is trouble sleeping and decreased appetite. At this point in AK’s life, the decreased appetite he is experiencing is bothersome to him. Low doses of mirtazapine can help with trouble sleeping and may also help increase his appetite. Should AK live longer than 2 months, the mirtazapine may also help with AK’s worsening depression.
4. It would not be wrong to recommend increasing AK’s duloxetine dose; however, there is a chance if AK only lives 2 months or less this would not benefit the patient. Increasing the dose of duloxetine should be discussed and, if no contraindications, be considered in this patient.
5. It would be appropriate to recommend discontinuing simvastatin in this patient. Currently, simvastatin offers no improvement in quality of life in this patient with a life expectancy of <2 months.
6. Finally, AK mentioned in his social history that he regularly attended church prior to his illness worsening. You could offer to invite a chaplain or pastor from his home church to visit with him regarding any spiritual concerns AK may have.
Chapter Summary

The development of palliative and hospice care over the past decades has improved the quality of life for older adults afflicted with complex, chronic, usually terminal illnesses. As the elderly patient approaches death, many considerations must be taken into account. It is important to review a patient’s medications for appropriateness. As a pharmacist, it is also important to understand these signs and symptoms as well as understand management options available to relieve these symptoms. Many symptoms that accompany death may also occur months to years prior to death in the elderly population (e.g., pain, depression). These symptoms are often managed similarly; however, depending on a patient’s life expectancy, appropriate management strategies may differ.

It is also important to consider a patient’s cultural beliefs and spiritual background and concerns. Although limited evidence is available about the role of the pharmacist and spiritual care, research shows that patients do want their healthcare professional to enquire about their spiritual needs.

Self-Assessment Questions

1. What number of medications has been shown to increase the risk for adverse drug interactions by >80%?

2. Which is the most useful and flexible class of medications for treatment of pain in patients at the end of life? What are available options for treatment of neuropathic pain in the palliative care setting?

Clinical Pearls

- Teamwork in palliative care is important because it relies heavily on many different disciplines for knowledge, expertise, understanding, and resourceful thought. An interprofessional team is made up of experts who are team players able to adapt to changing needs of the patient. These types of teams benefit the patient and the family, as well as the team members themselves. The overall goal of palliative care is achievement of the best quality of life for patients with terminal illnesses. Given this goal, many improvements in quality of life and symptom control will come from medication therapy. This reinforces the vital role pharmacists have in hospice and palliative care and the fact that they should be integral members of the interprofessional team.

- A patient may be discharged from hospice if he or she improves and no longer needs hospice care. These patients are said to “flunk” hospice or to be “hospice graduates.” At age 80, Art Buchwald, a famous writer/columnist for the Washington Post, decided to forego hemodialysis and enrolled in hospice, expecting to die in a few weeks. However, his kidneys continued to function, and he left hospice after 5 months, wrote a book, appeared on several news shows, and described himself as a “poster boy” for the benefits of hospice. Older adults may improve when enrolled in hospice because aggressive, toxic treatments are stopped, and supportive care is initiated that may stabilize a patient who has been losing weight and growing more debilitated. These patients may re-enter hospice in the future if their chronic illness progresses so they are again determined to have a prognosis of 6 months or less.
3. Describe the phenomenon of sundowning in terminally ill patients. What would be an appropriate medication to recommend for treatment?

4. What class of medications is recommended as first-line treatment of depression in the elderly whose life expectancy is >2 months?

5. What medication could be recommended for first-line management of dyspnea in end-of-life care?

6. Distinguish between proportionate palliative sedation versus palliative sedation to unconsciousness versus ordinary sedation. What is the most common agent used for proportionate palliative sedation?

7. What do the letters of the EASE tool, used in counseling grief, represent?

8. What are the differences between palliative care, hospice, and comfort care?

9. How may understanding cultural differences help a pharmacist working with patients in palliative or hospice care?

10. How are medications evaluated differently for appropriate use in patients in palliative and hospice care?

References


17. Markowitz AJ, McPhee SJ. Spiritual issues in the care of dying patients “….It’s okay between me and God” [comment]. JAMA. 2006;296:2254.


PART II
Pharmacotherapy
Issues of Aging

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Learning Objectives

1. Assess the significance of orthostatic hypotension and hypertension, appropriate goals for blood pressure, and first-line treatment recommendations in the geriatric population.

2. Evaluate a geriatric patient for appropriate lipid management.

3. Recognize potential barriers in diagnosis and treatment of peripheral arterial disease in geriatrics and the considerations that must be taken when treating intermittent claudication.

4. Describe the benefits versus risks of anticoagulation for stroke prevention in elderly patients with atrial fibrillation.

5. Discuss the evidence base for using beta blockers, angiotensin-converting enzyme (ACE) inhibitors, diuretics, and digoxin in geriatric heart failure patients as well as appropriate considerations when administering these drugs to geriatric patients.

6. Describe the significance of stroke in geriatric patients and recommend appropriate primary and secondary stroke prevention.

7. Explain the appropriate and safe use of anticoagulants for prevention and management of venous thromboembolism in elderly patients.

Key Terms and Definitions

ANTITHROMBOTIC: Prevents or interferes with the formation of a thrombus (clot).

DIGOXIN TOXICITY: Occurs when concentrations of digoxin increase above desired therapeutic levels. Arrhythmias are the most common manifestation and can be life threatening, especially in heart failure. Toxicity usually occurs in concentrations of >2 ng/mL but can occur at any level. The elderly are predisposed to toxicity.

FIBRINOLYTIC: A pharmacological intervention that dissolves an existing clot.
**INTERMITTENT CLAUDICATION**: A complication of peripheral arterial disease that presents as pain and fatigue caused by ischemia of muscles, usually in the lower extremities and typically brought on by walking.

**ISCHEMIC STROKE**: A type of stroke caused by a blood clot from a cardiac or noncardiac source that cuts blood flow off to a certain portion of the brain, causing tissue cell death.

**LEFT VENTRICULAR FUNCTION**: Measure of how well the left ventricle is contracting and expelling blood to the aorta. Also known as systolic function and often measured by ejection fraction.

**PULSE PRESSURE**: The difference between the systolic and diastolic blood pressures.

**THROMBOLYTIC**: See Fibrinolytic.

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**Introduction**

Cardiovascular diseases affect a large number of individuals in the United States each year. The prevalence and incidence of major cardiovascular diseases increase with advancing age. In many instances, there are issues related to management of specific cardiovascular diseases, safety of medications used to manage cardiovascular conditions, adherence to therapy, and others that are particularly pertinent in the elderly population. In this chapter, the epidemiology, etiology, clinical presentation, standard treatment, and treatment/safety issues associated with major cardiovascular diseases in elderly patients will be discussed. These will include orthostatic hypotension, hypertension, dyslipidemia, acute coronary syndromes and coronary artery disease, peripheral artery disease, heart failure, atrial fibrillation, stroke, and venous thromboembolism.

**Orthostatic Hypotension**

**Etiology, Epidemiology, and Clinical Presentation in the Geriatric Population**

Orthostatic hypotension is defined as a reduction in systolic blood pressure (SBP) of ≥ 20 mmHg or a reduction in diastolic blood pressure (DBP) of ≥10 mmHg within 3 minutes of standing. Some evidence indicates that the prevalence of orthostatic hypotension increases with age, although the data are equivocal. The prevalence of orthostatic hypotension in individuals >65 years of age is approximately 20% and is as high as 30% in individuals >75 years of age. The prevalence of orthostatic hypotension has been estimated to be as high as 50% in the frail elderly residing in nursing homes.

Rather than having lower baseline blood pressures, elderly patients who develop orthostatic hypotension often have developed age-related increases in supine SBP. In the National Health and Nutrition Examination Survey II, the relationship between postural changes on blood pressure and age and SBP was evaluated in 8,574 Caucasian, nondiabetic individuals between the ages of 25 and 74 years. Logistic regression analysis revealed that age was not associated with postural changes in blood pressure (relative odds 1.07, 95% confidence intervals [CI] 0.89–1.19 for each 10-year increase in age). However, increases in supine SBP were associated with postural changes in blood pressure (relative odds 1.59, 95% CI 1.49–1.70 for each 10-mmHg increase in SBP). It has been suggested that the association between age-related increases in supine blood pressure and increased risk of orthostatic hypotension may be due to central autonomic degeneration, resulting in baroreflex dysfunction in the presence of residual sympathetic outflow.

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**Key Point**: Orthostatic hypotension that develops in association with advancing age is directly correlated with age-related increases in supine SBP.
Orthostatic hypotension may be classified as acute or chronic. Acute orthostatic hypotension develops over a short period of time. Causes of acute orthostatic hypotension include dehydration, diarrhea, extreme heat, myocardial ischemia, adrenal insufficiency, vomiting, or, more rarely, sepsis. Importantly, acute orthostatic hypotension may be caused by medications, including antihypertensive agents. Antihypertensives that are more likely to cause orthostatic hypotension are those that are short acting, vasodilators, or volume depleting. These include centrally acting alpha receptor agonists, peripheral alpha receptor antagonists, nitrates, and other vasodilators such as hydralazine or minoxidil, and loop diuretics. Other medications that can cause this include antipsychotic drugs, dopamine agonists, levodopa, marijuana, narcotics, sedatives, sildenafil, and tricyclic antidepressants.2

Chronic orthostatic hypotension develops gradually over a more prolonged period of time. It may develop as a result of pathophysiological changes, including diminished baroreceptor sensitivity, diastolic dysfunction, or development of hypertension. In addition, chronic orthostatic hypotension may arise due to dysfunction of the autonomic nervous system, from causes such as brain stem lesions, Lewy Body dementia, multiple cerebral infarctions, myelopathies, Parkinson disease, or multiple system atrophy.2 Other etiologies of orthostatic hypotension may include increased venous insufficiency, alcoholism, amyloidosis, diabetes mellitus, and pernicious anemia.2 Orthostatic hypotension may be more likely in patients with a low body mass index.5

Most patients with orthostatic hypotension experience symptoms associated with postural change, including dizziness, lightheadedness, weakness, pre-syncpe, syncope, blurred vision, nausea, dyspnea, neck pain, angina, and transient ischemic attacks.1,2 Elderly patients are particularly susceptible to symptoms such as slurred speech, falls, confusion, and cognitive impairment. In some patients, symptoms may be worsened by prolonged standing, exercise, increased ambient temperature, or eating. Orthostatic hypotension is a common cause of hospitalization. In 2004, there were nearly 81,000 hospitalizations related to orthostatic hypotension.

**Treatment Recommendations in the Geriatric Population**

Because orthostatic hypotension most commonly occurs in elderly patients, the treatment recommendations for all adults are written with the elderly in mind. If the orthostatic hypotension is believed to be drug-induced, therapy with the causative agent should be discontinued. Patients should be advised to rise slowly from a sitting or supine to a standing position, particularly individuals that have undergone long periods of inactivity or bedrest. Patients should be counseled to avoid coughing, straining, or prolonged standing, especially in hot weather, as these activities reduce venous return to the heart.2 Crossing the legs while standing and contracting muscles for 30 seconds may increase venous return. Raising the head of the bed by 20–30 degrees may minimize hypertension and overnight volume loss. Use of waist-high compression stockings and abdomen-binders may be helpful, as may increasing sodium and water intake.2 Hypertension is a risk factor for orthostatic hypotension, and maintaining adequate control of elevated blood pressures may help prevent orthostatic hypotension from occurring or worsening.

Nonpharmacological management and hypertension control are the preferred methods to help prevent and alleviate symptoms of orthostatic hypotension. Medications for orthostatic hypotension should only be used in select cases when other methods for symptoms have been exhausted. Drugs that are most often used for the management of orthostatic hypotension are fludrocortisone and midodrine. Fludrocortisone is a synthetic mineralocorticoid agent that promotes fluid and sodium retention.1,2 The initial recommended dose of fludrocortisone is 0.1 mg orally daily. The dose may be titrated upward in weekly increments of 0.1 mg daily if neces-
sary, until the maximum dose of 0.3 mg daily is attained, or pedal edema occurs. Adverse effects of fludrocortisone include supine hypertension, ankle edema, headache, hypokalemia, and, rarely, heart failure in susceptible patients. Elderly patients may be more susceptible to some of the adverse effects associated with fludrocortisone, particularly fluid overload and hypokalemia. Many elderly patients receiving this drug may require potassium supplementation, especially those taking higher doses.

In patients who continue to exhibit symptoms despite therapy with fludrocortisone, or in those patients in whom fludrocortisone is poorly tolerated, midodrine is a reasonable alternative. Midodrine is a peripheral selective alpha-receptor agonist. The initial recommended midodrine dose is 2.5 mg orally three times daily during daytime hours; if necessary, the dose may be titrated upward in weekly increments of 2.5 mg per dose, until the maximum recommended dose of 10 mg three times daily is reached. Adverse effects of midodrine include supine hypertension, pruritus, paresthesias, piloerection, bradycardia, and urinary retention. Midodrine should not be administered to patients with a history of coronary artery disease, heart failure, urinary retention, acute kidney disease, or thyrotoxicosis. In addition, the risk of midodrine-associated bradycardia is increased when the drug is used concomitantly with other heart rate-lowering drugs, such as beta blockers, diltiazem, verapamil, amiodarone, or digoxin. Increasing caffeine intake up to doses of 200 mg may be an effective intervention as well.

**Barriers to Treatment in the Geriatric Population**

There are few barriers to treatment in the geriatric population, once a diagnosis of orthostatic hypotension has been made. However, appropriate recognition and diagnosis can be difficult. Blood pressure measurements are routinely performed with patients in the sitting position, limiting the ability to diagnose orthostatic hypotension. Clinicians should be aware of the potential for orthostatic hypotension in older patients and should be alert to detect symptoms. The Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (JNC) VII recommends that supine and standing blood pressure be measured periodically in all hypertensive patients >50 years of age. The new JNC VIII guidelines do not make a specific recommendation in measuring orthostatic blood pressure. The ACCF/AHA 2011 Expert Consensus on Hypertension in the Elderly recommend a sitting blood pressure and blood pressure taken within 1–3 minutes of standing in those ≥65 years of age.

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**Hypertension**

**Etiology, Epidemiology, and Clinical Presentation in the Geriatric Population**

Cardiovascular disease (CVD) is the leading cause of mortality among individuals over the age of 65 years. Hypertension is one of the most prevalent and important risk factors contributing to CVD among adults. The prevalence of hypertension increases with advancing age, with elevated SBP of particular importance. Stratifying populations of elderly patients based on age reveals that 8% of the population over the age of 60 years has elevated SBP, while 25% of the population over the age of 80 years has elevated SBP. Women 65 years and older have a higher prevalence of hypertension than men of the same age. Despite this increase in prevalence with age, it may not be accurate to assume that hypertension correlates with the increasing incidence of CVD events and mortality in all age subsets of elderly patients. A divergence in clinical outcomes has been observed among individuals with hypertension who are over 65 years of age as compared with those over 85 years.

In patients between the ages of 65 and 84 years, survival rates are lowest in those individuals with SBP >180 mmHg. However, in patients over the age of 85 years, differences in survival rates in those with SBP <130 mmHg compared to those with SBP >180 mmHg are less clear.
One study evaluated the relationship between blood pressure and survival in patients over the age of 85 years, found that the risk of death was actually highest among individuals with SBP <140/90 mmHg, who would have been defined as “at goal” per JNC VII guidelines.6,10

The relationship between DBP and risk may also change with age. Physiologically, DBP decreases with normal aging due to the decreased ability of vessels to expand during systole and contract during diastole. A negative relationship has been demonstrated between lower DBP and total mortality.9 In a population of 7,557 patients over the age of 60 (average age of 70 years), lower DBP was associated with increased mortality rates across all strata of SBP.11 This suggests that a high pulse pressure may be a predictive factor of CVD events in this population.

Elderly patients may also have more variation in their blood pressure readings than younger patients. This is referred to as labile hypertension and may be due to loss of elasticity of arterial walls, changing the manner in which baroreceptors respond.12 Labile hypertension has not been proven to be an independent risk factor for cardiovascular disease.13 However, in patients with labile hypertension, these blood pressure variations emphasize the need for several blood pressure measurements to be taken, including home readings, prior to treatment decisions. Decreased renal function and ability to excrete salt loads occur with age.8 These changes can create salt sensitivity and make diet history a very important part of a patient history in the elderly, as well as a salt reduction as a treatment target.

Based on these data, the association between hypertension and CVD outcomes among individuals over the age of 60 is well established. However, it appears that the association between treating hypertension and CVD outcomes is not as clear among the strata of elderly patients who are of extremely advanced age, in whom high pulse pressures may actually be associated with increased mortality. Therefore, the optimal blood pressure goal across all strata of older individuals remains somewhat unclear.

**Standard Adult Treatment Recommendations**

The standard of care for the treatment of hypertension in the adult population has been well established by the JNC VII guidelines.6 The new JNC VIII guidelines, released in late 2013, changed blood pressure goals for many situations and were met with some controversy and criticism.7 The American College of Cardiology and American Heart Association will likely be releasing a new guideline on blood pressure management some time in 2015 for clinicians because they did not endorse JNC VIII. One of the major changes in the new JNC VIII is that the SBP goal for those 60 years and older was set at 150 mmHg.7 The previous goal was 140 mmHg in JNC VII. Some of the authors of the new JNC VIII have disagreed with their own guidelines on this recommendation, after the guidelines were published. The SBP goal remains <140 mmHg for those younger than 60 years in and the diastolic goal remains 90 mmHg.7 The <140/90 mmHg target was also extended to diabetes and chronic kidney disease (CKD) patients.7 JNC VIII recommends starting pharmacological treatment with a thiazide diuretic, ACE inhibitor, angiotensin receptor blocker (ARB), or calcium channel blocker. In the African American population, a thiazide diuretic or calcium channel blocker are preferred as initial therapy, unless patients have CKD or diabetes, due to the reduced efficacy of other agents in this population. All other medications are to be used later in treatment, unless they have a compelling indication.

Goal blood pressure can be achieved with monotherapy or combination drug therapy, although the guidelines recommend that medication therapy should be initiated at low doses and titrated slowly to avoid orthostatic hypotension, to which elderly patients are more susceptible. The acceptance and implementation of JNC VIII into clinical practice is still undetermined. Some clinicians are still referring to JNC VII and await the ACC/AHA guidelines in the near future.
Treatment Recommendations in the Geriatric Population

While current guidelines are well supported with randomized clinical trials, it is reasonable to examine whether these recommendations apply to all subgroups in the elderly population. To determine this and to select specific medications that are the best choices for treatment, one must consider the literature on which the JNC VII and JNC VIII recommendations for older patients are based. Specifically, the clinical trials that included at least some elderly patients who also met criteria for inclusion in the JNC VIII guidelines include the Systolic Hypertension in the Elderly Program (SHEP), the Swedish Trial in Old Patients with Hypertension (STOP), the Systolic Hypertension in Europe (Syst-Eur), and the Medical Research Council (MRC) trial. Collectively, these trials enrolled patients with an average age of 74 years. Study populations were large, ranging from 1,627 to 4,736 subjects. All of the trials lasted at least 2 years and showed a reduction in the risk of endpoints such as stroke or cardiovascular death.

The Hypertension in the Very Elderly Trial (HYVET) was also included in the analysis for the new JNC VIII guidelines. HYVET enrolled 3,845 subjects over the age of 80 years, with an average follow-up period of 21 months. The baseline SBP was 173/90 mmHg in the treatment and control groups, and the treatment blood pressure goal was <150/90 mmHg. The treatment intervention was a diuretic or placebo, with the possible addition of an ACE inhibitor in the treatment group. The results showed a significant decrease in rate of fatal/nonfatal stroke (30%), incidence of death from stroke (39%), rate of death from any cause (21%), and incidence of heart failure (64%) associated with antihypertensive therapy. The benefits began to appear in the treatment group at 1 year. Limitations of the trial included the fact that, based on demographic characteristics of patients enrolled, the elderly population enrolled in this study was likely healthier than the typical elderly population. Therefore, the results may not be applicable to the frail elderly population. Exact causes of death were difficult to validate in some cases; evidence was required to classify as a death from stroke. Rapid, unexpected deaths were classified as cardiac causes. Nonetheless, the incidence of death from all causes was significantly reduced in the antihypertensive treatment group. This study also demonstrated that thiazide diuretics, with or without the addition of an ACE inhibitor, have been associated with the favorable outcomes among patients of advanced age.

Based on evidence from these trials, blood pressure goals established for the adult population are likely appropriate for patients over the age of 65 and remain valid endpoints throughout the seventh decade of life. The criticism that the goal for those 60–80 years should have remained <140/90 mmHg is still being debated, and in 2015, with the release of the ACC/AHA guidelines, this may be clarified further. With the inclusion of the HYVET trial into JNC VIII, the blood pressure goal of <150/90 mmHg in the new guidelines is also probably a valid goal for those 80 years and older as well. This blood pressure goal is also supported by other international guidelines for those over 80 years. The Canadian Hypertension Education Program and the European Society of Hypertension/European Society of Cardiology 2013 guidelines both recommend a blood pressure goal of <150/90 mmHg for those 80 years and older. Given these controversies, decisions about antihypertensive medication and target blood pressure should be guided by the presence of other cardiovascular risk factors and non-cardiovascular co-morbidities and individualized for each older adult.

Blood pressure assessment in the elderly has some special consideration that clinicians should keep in mind. Sclerotic arteries are more difficult to compress with the blood pressure cuff. This can result in falsely elevated blood pressure readings. Auscultatory gap and white-coat hypertension is also more common in the elderly. Standing blood pressures should always be measured due to risk of orthostasis. The ACCORD BP trial was taken into account in the 2011 ACC/AHA consensus document on
hypertension in the elderly. This trial showed no additional benefit with a systolic BP of 120 mmHg versus 140 mmHg in high-risk patients over 55 years with diabetes.\textsuperscript{20} In fact, there were increased adverse effects from the antihypertensives in this group. The 2011 ACC/AHA consensus document on hypertension in the elderly recommended a SBP of 140–145 mmHg for those 80 years and older. They also recommend SBPs under 130 mmHg and diastolic under 65 mmHg be avoided in those over 80 years.\textsuperscript{8}

When looking at all of the recent evidence and guidelines released over the past few years, it seems reasonable to target a blood pressure of $<$150/90 mmHg in those 80 years and over. In those younger than 80 years the new JNC VIII document would suggest the same goal; however, many still believe the $<$140/90 mmHg is the better target. Both JNC VII and VIII included a fair number of patients who were between 65 and 80 years. Blood pressure targets and treatment should always have risks and benefits assessed rather than using a “one goal/treatment fits all” approach.

The JNC VIII recommendation for first-line choice of pharmacologic therapy applies to the entire adult population, including the elderly population. It was noted in JNC VIII that in those older than 75 years with CKD, there was no evidence that using an ACE inhibitor or ARB improved kidney outcomes.\textsuperscript{7} These agents can still be used in those older than 75 years, but a thiazide diuretic or calcium channel blocker are also reasonable first-line choices in this population. Considerations for the use of some of the common antihypertensive classes in the geriatric population are listed in Table 7-1.

**Barriers to Treatment of the Geriatric Population**

Patients older than 75 years are not as likely to receive counseling on lifestyle recommendations compared to younger adults.\textsuperscript{8} Given the potential for salt-sensitive hypertension discussed above, lifestyle recommendations should be implemented in all patient age groups. Salt restriction can be an important part of treatment for those 65 years and over who are consuming large quantities of salt in their diet and who have no history of hypotension. The Trial of Nonpharmacologic Interventions in the Elderly (TONE) studied sodium reduction and weight loss as interventions for hypertension in those 60–80 years old. Salt intake was limited to less than 1800 mg/day and participants lost an average of 3.9 kg in a little over 2 years. Both of these interventions led to significant blood pressure reductions, with some patients being able to discontinue antihypertensives.\textsuperscript{21} A decreased ability to taste salty foods may occur with aging, as well as a lack of transportation to obtain fresh fruits and vegetables on a regular basis. Lifestyle recommendations are important in elderly patients because they may help to avoid medications in some cases.

Adverse outcomes can be associated with failure to initiate an appropriate dose and titrate on an appropriate schedule. Therapeutic goals, frailty, patient prognosis, and age-related decline in kidney function must be considered when initiating and titrating therapy; although once a maintenance dose has been achieved, the reduction of antihypertensive medication based on age or creatinine clearance (CrCl) is inappropriate without an assessment of whether the patient has been tolerating the regimen and has achieved the desired therapeutic goal. Instead, increasing the frequency of monitoring may be prudent. For example, elderly patients with reduced CrCl are particularly vulnerable to hyperkalemia associated with ACE inhibitors, requiring increased frequency of serum chemistry monitoring. Due to age-related changes in pharmacokinetics and pharmacodynamics, some classes of antihypertensive medication, including beta blockers, centrally acting alpha-agonists, peripheral alpha-agonists, nitrates, and other vasodilators present special concerns for older patients, as noted in Chapter 3.\textsuperscript{22}
Table 7-1. Characteristics of Common Classes of Antihypertensives Used in the Elderly

<table>
<thead>
<tr>
<th>Antihypertensive Class</th>
<th>Compelling Indications</th>
<th>Adverse Effects</th>
<th>Route of Elimination/Dosing Adjustments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alpha-1 adrenergic blockers</td>
<td>Benign prostatic hypertrophy</td>
<td>Orthostatic hypotension</td>
<td>Hepatic: start at lowest dose and titrate</td>
</tr>
<tr>
<td>ACE inhibitors and angiotensin II receptor blockers</td>
<td>Heart failure, post-MI, CKD, diabetes</td>
<td>Hyperkalemia, cough, angioedema, renal impairment</td>
<td>ACE inhibitors:</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>• Renal: start at lowest dose and titrate</td>
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<td>» fosinopril is both hepatic and renal</td>
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<td></td>
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<td></td>
<td>Angiotensin II receptor blockers:</td>
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<td></td>
<td></td>
<td></td>
<td>• Hepatic: no dose adjustment</td>
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<td></td>
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<td>» candesartan and eprosartan are both</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>hepatic and renal</td>
</tr>
<tr>
<td>Beta adrenergic blockers</td>
<td>Heart failure, post-MI, atrial fibrillation rate control, essential tremor, migraine</td>
<td>Bradycardia, fatigue, bronchospasm</td>
<td>Renal: initiate at lowest dose and titrate:</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>• nadolol, atenolol, carvedilol, nebivolol</td>
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<td></td>
<td></td>
<td></td>
<td>Hepatic: initiate at lowest dose and titrate:</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>• propranolol, metoprolol, labetalol, nebovilo</td>
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<tr>
<td>Calcium channel blockers</td>
<td>Atrial fibrillation rate control (nondihydropyridine)</td>
<td>Nondihydropyridine: exacerbation of GERD, gingival hyperplasia, constipation (verapamil), heart block, bradycardia</td>
<td>Hepatic: start at lowest dose and titrate</td>
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<tr>
<td></td>
<td></td>
<td>Dihydropyridine: peripheral edema</td>
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<tr>
<td>Loop diuretics</td>
<td>Heart failure</td>
<td>Hyponatremia, hypokalemia</td>
<td>Renal: no dose adjustment</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>• furosemide, bumetanide</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>Hepatic: no dose adjustment</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>• bumetanide, torsemide</td>
</tr>
<tr>
<td>Thiazide diuretics</td>
<td>Osteoporosis</td>
<td>Gout, hyponatremia, hypokalemia</td>
<td>Renal: no dose adjustment needed</td>
</tr>
</tbody>
</table>

ACE, angiotensin-converting enzymes; CKD, chronic kidney disease; GERD, gastroesophageal reflux disease; MI, myocardial infarction.
**Lipid Management**

**Etiology, Epidemiology, and Clinical Presentation in the Geriatric Population**

Approximately 25% of adults have elevated plasma low-density lipoprotein (LDL) concentrations. Roughly 63% of patients with elevated plasma LDL concentrations are aware of the condition, and about 41% of those with elevated LDL are taking lipid-lowering medications.

Serum concentrations of total cholesterol and LDL increase throughout life, and hyperlipidemia is a common condition in elderly patients. Published data indicate that the risk associated with elevated plasma cholesterol concentrations observed in younger patients persists in the elderly. In a multicenter, longitudinal study of 4,066 men and women 65 years of age or older (average age 79.2 years at initiation of study), there was a significant correlation between increasing plasma cholesterol concentrations and the increased adjusted relative risk of death due to coronary heart disease over a 4-year period. In addition, in a prospective cohort study of patients 80 years and older, higher plasma high-density lipoprotein (HDL) concentrations were shown to be associated with survival during a 2-year period. Men who survived during this period had mean plasma HDL concentration of 43.4 ± 10.3 mg/dL, compared with 36.7 ± 7.6 mg/dL in those who died (p = 0.001). Similarly, women who survived had higher plasma LDL concentrations than those who did not (49.3 ± 14.9 mg/dL versus 42.2 ± 11.5 mg/dL, p = 0.001).

A meta-analysis of 61 prospective observational studies that enrolled almost 900,000 adults was performed to determine the relevance of blood pressure and total cholesterol on vascular mortality. The investigators reported that a prolonged reduction in total cholesterol concentration of 1 mmol/L (38.6 mg/dL) from mean usual concentrations was associated with the following age-related reductions in the hazard ratio (HR) for death due to ischemic heart diseases: age 40–49 years, HR 0.44 (95% CI 0.42–0.48); age 50–59 years, HR 0.58 (0.56–0.61); age 60–69 years, HR 0.72 (0.69–0.74); age 70–79 years, HR 0.82 (0.80–0.85); 80–89 years, HR 0.85 (0.82–0.89). Therefore, while the magnitude of reduction in HR for death due to ischemic heart disease diminished in patients between the ages of 70–79 years and 80–89 years, the reduction in hazard remained statistically significant in both groups. In addition, there was a strong and significant inverse relationship between plasma HDL concentration and hazard of death due to ischemic heart disease in every age group. Paradoxically, the HR for ischemic stroke associated with a 1-mmol/L (38.6-mg/dL) lowering of plasma cholesterol concentration compared to usual values was reduced only in patients between the ages of 40–59 years, and it was increased in patients between the ages of 80–89 years (HR 1.06, 95% CI 1.00–1.13). The investigators were unable to explain the absence of an independent positive association of cholesterol with stroke mortality at older ages.

**Standard Adult Treatment Recommendations**

Treatment recommendations for hyperlipidemias are based on the 2013 ACC/AHA Guide on the Treatment of Blood Cholesterol to Reduce Atherosclerotic Cardiovascular Risk in Adults, which came out in late 2013. These new guidelines represent a very different approach to prescribing drug therapy for hyperlipidemia. Four statin benefit groups were identified to help clinicians decide which of their patients would benefit from statins. All statins were also divided into low-, moderate-, and high-intensity doses. Goals for LDL and other lipid parameters were not used in the new guidelines, which focus on an appropriate intensity for certain risk groups. The four groups that were identified to benefit from statins include (1) those with arteriosclerotic cardiovascular disease, (2) those with LDL ≥190 mg/dL, (3) those between the ages of 40–75 years with diabetes, and (4) those with a ≥7.5% estimated 10-year risk between the ages...
of 40–75 years old. A new Pooled Cohort Equation was developed to calculate this 10-year risk, which is different than the previous Framingham equation used.\textsuperscript{27} In general, use of lipid-lowering medications other than statins was discouraged in the new guidelines due to the lack of benefit on cardiovascular outcomes in recent studies with these agents.\textsuperscript{27}

Standard treatment still includes therapeutic lifestyle changes to reduce the dietary intake of saturated fats, weight reduction, and increasing physical activity.\textsuperscript{27} These lifestyle recommendations should be implemented in everyone but are no longer recommended to reduce LDL before drug therapy is initiated. If drug therapy is indicated, it should be initiated concurrently.

**Treatment Recommendations in the Geriatric Population**

Relatively few studies have been conducted to determine the benefits associated with management of hyperlipidemias in the elderly, especially those over age 80. The new guidelines focused exclusively on randomized controlled clinical trials. There were few people in these trials older than 75 years. Data from secondary prevention trials showed support for continuation of statins in patients age 75 and older as well as benefits in initiating statins in this age group. Interestingly, the new guidelines recommend moderate-intensity statin therapy in those over age 75 instead of the high intensity recommended for secondary prevention in all others. This was supported by the small amount of data available in this age group, showing that titration to high intensity did not provide better outcomes. Patients age 75 or older, with or without diabetes, should have risks and benefits weighed to determine whether statin therapy should be initiated. The guidelines focus on the discussion of these risks and benefits between the clinician and patient. The Pooled Cohort Equations can estimate 10-year risk in patients aged 76–79 that can be used as a factor in this decision. Age is a strong predictor of 10-year risk in the new equation, with a large number of elderly patients meeting the criteria for statin use in primary prevention based on this calculation. This again places emphasis on the need for older adults to have a risk versus benefit discussion with their care provider. Other factors to weigh in primary prevention in those older than 75 include drug-drug interactions, risk of adverse effects, atherosclerotic cardiovascular disease (ASCVD) reduction benefits, current disease states, life expectancy, and patient preference.\textsuperscript{27}

One of the few trials to specifically evaluate treatment of dyslipidemia in the elderly is the pravastatin in elderly individuals at risk of vascular disease (PROSPER) trial.\textsuperscript{28} It randomized 5,804 patients between the ages of 70–82 with a history of or risk factors for vascular disease to receive therapy with pravastatin 40 mg daily or placebo. The mean serum LDL concentration in randomized patients was 147 ± 31 mg/dL. In patients randomized to receive pravastatin, serum LDL concentrations were relatively reduced (34%), and the incidence of primary endpoint events (composite endpoint of death from coronary heart disease, nonfatal myocardial infarction [MI], and fatal or nonfatal stroke) was reduced by 15% in pravastatin-treated patients. Pravastatin therapy was not associated with a significantly greater deterioration of cognitive function than placebo, and there was no significant difference between the groups in the incidence of myalgias. Overall, the results of the PROSPER trial support that elderly patients appear to benefit from lipid-lowering therapy, both those with vascular disease or those merely at risk.

The Justification for the Use of Statins in Prevention: an Intervention Trial Evaluating Rosuvastatin (JUPITER) study looked at primary prevention with rosvuvastatin. The original trial looked at patients with an LDL <130 mg/dL.\textsuperscript{29} A subgroup analysis of 5,695 patients 70 years and older was done to evaluate primary prevention in the elderly. There was a significant reduction in occurrence of first cardiovascular event in the rosvuvastatin group in those 70 years and older. Absolute reduction was greater in this elderly group as well.\textsuperscript{30} One must take into account that the JUPITER trial was not designed initially to evaluate primary prevention in those 70 years
and older, but it is another piece of encouraging evidence for some benefit in primary prevention that can be considered in the treatment discussion with patients.

Barriers to Treatment in the Geriatric Population

Elderly patients may be at increased risk of developing statin-induced myopathy, particularly those over age 75. In addition to age, risk increases with polypharmacy, reduced renal function, and female sex, all common characteristics of many elderly patients. Consequently, elderly patients must be counseled regarding the symptoms of statin-induced myopathy, advised to seek medical attention should symptoms develop, and be diligently questioned regarding potential symptoms during routine follow-up visits.

A series of case reports to the Food and Drug Administration (FDA) between 1997 and 2002 reported confusion or memory loss with the use of statins. The lipophilic statins, simvastatin and atorvastatin, had more reports in the case series. Several cases of the memory loss resolved after stopping the statin. If an elderly patient reports memory loss soon after starting a statin, it would be reasonable to stop the statin and assess it as the cause. Other causes of memory loss in the elderly are more common than that caused by statins and should also be evaluated as possible etiology.

Statins are still reported as underutilized in some populations of older patients. Age itself is not a contraindication to statin therapy, nor is nursing home placement. Factors such as frailty, advanced dementia, or patient preferences for palliative-only interventions are often a reason to defer or discontinue drug therapy. In such instances, strict diets and other lifestyle restrictions are also often relaxed or abandoned. This is discussed further in Chapter 6.

Acute Coronary Syndromes/Coronary Artery Disease

Etiology, Epidemiology, and Clinical Presentation in the Geriatric Population

Coronary artery disease is the leading cause of death in the United States and throughout the world, particularly in the elderly population. The average age at which individuals experience a first MI is 66 for men and 70 for women. Acute coronary syndromes (ACS) account for roughly 35% of all deaths among individuals ≥65 years of age. Eighty-three percent of all individuals who die from ischemic heart disease are >65 years of age. Although only 6% of the population of the United States is >75 years of age, 60% of all deaths related to MI occur in that population. In addition, elderly patients are at higher risk for adverse outcomes associated with ACS. For each 10-year increase in age, the odds of in-hospital mortality associated with ACS increase by 70%. Greater than 50% of patients ≥75 years of age develop heart failure due to systolic or diastolic dysfunction following an MI.

Patients with an ACS typically present with crushing, squeezing substernal chest discomfort that may be accompanied by pain and discomfort in the arm, back, or jaw. Additional symptoms may include nausea, vomiting, or shortness of breath. Elderly patients are more likely to present with atypical symptoms than younger patients. A higher proportion of elderly patients experiencing an MI complain of dyspnea, diaphoresis, nausea and vomiting, and syncope as primary complaints compared with younger patients, while a substantially lower proportion of elderly patients complain of chest discomfort. Some elderly patients experiencing an MI may be completely asymptomatic. This renders the diagnosis of MI more difficult in the
elderly. Serum troponin I and/or creatine kinase concentrations are elevated in patients experiencing an MI. Some patients demonstrate elevated ST segments on the electrocardiogram (ST-segment elevation MI [STEMI]), while others do not (non-ST segment elevation MI [NSTEMI]). Elderly patients with ACS are more likely than younger patients to present with nondiagnostic electrocardiograms (ECGs).

**Standard Adult Treatment Recommendations**

(a) STEMI: Standard treatment recommendations for the adult population can be found in the 2013 ACCF/AHA Guideline for the Management of ST-Elevation Myocardial Infarction. Initial therapy includes oxygen (if the oxygen saturation is <90%), sublingual nitroglycerin, aspirin 162–325 mg orally, and intravenous (IV) nitroglycerin. Morphine should also be administered for relief of pain and anxiety. A P2Y12 receptor blocker should be administered to all patients, as well as reperfusion therapy with primary percutaneous intervention (PCI) or fibrinolysis (alteplase, reteplase, tenecteplase, or streptokinase) with an appropriate anticoagulant. In patients who undergo primary PCI, adjunctive therapy with unfractionated heparin and abciximab or bivalirudin should be administered.

(b) NSTEMI: Standard recommendations for the adult population can be found in the 2011 ACCF/AHA Focused Update of the Guidelines for the Management of Patients with Unstable Angina/Non-ST-Elevation Myocardial Infarction. Initial therapy includes oxygen (if the oxygen saturation is <90%), sublingual nitroglycerin, aspirin 162–325 mg orally, and IV nitroglycerin (Table 7-1). Morphine should also be administered for relief of pain and anxiety. Patients should receive IV unfractionated heparin or subcutaneous enoxaparin, fondaparinux, or bivalirudin. A P2Y12 receptor blocker should be administered to all patients. In those patients who receive bivalirudin, the use of Gb IIb/IIA inhibitors is not recommended. (See the guidelines for more specific recommendations on antiplatelet and anticoagulant therapy.)

(c) Secondary prevention of coronary events: To reduce the risk of subsequent coronary events, patients with documented coronary artery disease should receive aspirin 75–162 mg daily, indefinitely. For patients who undergo PCI with placement of a bare metal stent, the aspirin dose should be 162–325 mg daily for a minimum of 30 days; for a sirolimus-eluting stent, 162–325 mg daily for 3 months; for a paclitaxel-eluting stent, 162–325 mg daily for 6 months; in all cases, the aspirin dose should be 75–162 mg daily thereafter, indefinitely. Patients with NSTEMI who are managed medically should receive clopidogrel 75 mg orally or prasugrel 10 mg daily for a minimum of 12 months. For patients who undergo PCI with placement of a stent, clopidogrel or prasugrel should be administered for a minimum of 12 months. All patients should receive long-term therapy with an oral beta blocker, ACE inhibitor, or ARB, and lipid-lowering therapy. Prasugrel should not be given to patients with a history of stroke or transient ischemic attack due to increased bleeding risk, and its FDA-required labeling also carries a warning against use in patients over 75 years of age, citing increased risk of intracranial bleeding and uncertain benefit.

**Treatment Recommendations in the Geriatric Population**

Although some studies have been conducted regarding the efficacy of specific treatment strategies in the elderly, many trials of pharmacological interventions for ACS and secondary prevention have included relatively small populations of elderly patients. This has resulted in some cases in a lack of data regarding the safety and efficacy of specific pharmacological therapy in the elderly. Much more research regarding the efficacy of management strategies for ACS and secondary prevention of ACS in elderly patients is needed.

(a) STEMI: Relatively few studies have described the efficacy of treatment strategies in elderly patients with STEMI. Data from small randomized studies suggest that PCI is more effective than fibrinolytic therapy for reducing
the incidence of reinfarction and need for target vessel revascularization in elderly patients. The efficacy of PCI and fibrinolytic therapy appear similar within the first 3 hours following symptom onset, but PCI is more effective in elderly patients who present >6–12 hours following symptom onset.39

Because many hospitals do not have cardiac catheterization laboratories, fibrinolytic therapy remains a viable option in patients with STEMI. Some data indicate that the elderly population may derive a larger degree of mortality reduction associated with fibrinolytic therapy than younger populations.39 Advanced age is not a contraindication to receive fibrinolytic therapy, as mortality benefit has been demonstrated in patients up to 85 years of age, despite the fact that age and age-related comorbidities are associated with an increased risk of fibrinolytic-associated intracranial hemorrhage. Therefore, fibrinolytic therapy should be administered to elderly patients up to the age of 85 years who do not have contraindications to therapy. Due to the increased risk of intracranial bleeding and the relative lack of data regarding the efficacy of fibrinolytic agents in patients older than 85, therapy with these drugs is not generally recommended, but further research is necessary.39 Either unfractionated heparin or low molecular weight heparin can be administered with fibrinolytic agents as adjunctive therapy in the elderly population. In patients ≥75 years of age, higher rates of intracranial hemorrhage have been reported with enoxaparin compared with those due to unfractionated heparin when used as adjunctive therapy with tenecteplase. However, when enoxaparin doses are adjusted appropriately for declining kidney function in the elderly, data suggest that enoxaparin may be more effective than unfractionated heparin as adjunctive therapy with fibrinolytics for improving outcomes. If clopidogrel is given with fibrinolytics, the loading dose of 300 mg should not be given to those older than 75 years.36,37

Some evidence suggests that elderly patients with STEMI may derive greater benefit associated with the administration of IV beta blockers than younger patients.39 However, these data apply to patients within the range of 65–75 years of age; the study did not include patients >75 years old. Other data suggest that patients with STEMI who are 70 years of age or older are particularly susceptible to the hypotensive and bradycardic effects of IV beta blockers and may be at greater risk of developing cardiogenic shock associated with these drugs. Therefore, administration of IV beta blockers to elderly patients experiencing STEMI with hemodynamic compromise is not recommended.39

(b) NSTEMI: Data regarding the magnitude of benefit associated with glycoprotein IIb/IIIa receptor inhibitors in elderly patients with NSTEMI are variable and equivocal. Older age has been identified as a risk factor for bleeding associated with glycoprotein IIb/IIIa receptor inhibitors. In addition, eptifibatide and tirofiban undergo renal elimination, and, therefore, the risk of bleeding associated with these drugs increases with worsening kidney function. In elderly patients, glycoprotein IIb/IIIa receptor inhibitors are associated with the greatest benefits when administered at the time of a PCI, and when the drugs are not administered to patients with kidney disease. Additional research regarding the benefits versus the risks of glycoprotein IIb/IIIa receptor inhibitors in patients with NSTEMI who are not undergoing PCI is needed.37

(c) Secondary prevention of coronary events: Subgroup analyses of elderly patient populations in randomized trials indicate that older patients may derive greater benefit from specific adjunctive therapies for secondary prevention. For example, oral beta blocker therapy is associated with a greater degree of reduction in the relative risk of reinfarction and mortality in elderly patients with a prior MI than in younger patients.39 Similarly, elderly patients derive greater reduction in risk of subsequent coronary events associated with aspirin therapy than younger patients. Secondary prevention with ACE inhibitors or ARBs is equally beneficial in elderly patients compared with younger patients.
Barriers to Treatment in Geriatric Population

As discussed, many elderly patients with ACS present with atypical symptoms and/or nondiagnostic ECGs, rendering the diagnosis of ACS more difficult. In addition, ACS is more likely to occur in elderly patients with a larger number of comorbid conditions, sometimes confusing the diagnosis. These factors often result in misdiagnosis or delays in diagnosis, which in turn delays appropriate treatment. Further, prehospital delays in seeking appropriate treatment for ACS are more likely in elderly patients, as a result of atypical or absent symptoms and socioeconomic or cognitive factors.39

The proportion of elderly patients with STEMI who are eligible for reperfusion therapy, either with fibrinolytic agents or PCI, is substantially lower than in younger populations, due to a higher prevalence of exclusion criteria. Overall, elderly patients are at higher risk for adverse effects associated with many agents used for the management of ACS or for secondary prevention, in part due to diminished kidney function. Many studies of pharmacological therapy for acute management of ACS and for secondary prevention have included only small numbers of elderly patients. Therefore, there is a relative lack of data regarding efficacy and safety of specific therapies, and this has led to under-use of life-prolonging drugs in the elderly, including fibrinolytic agents, beta blockers, ACE inhibitors, and others. Adherence to treatment guidelines in elderly patients should be strongly encouraged.

An extension of this issue includes use of dual antiplatelet therapy, which has also resulted in an increased risk for bleeding in older patients; clinicians may hesitate to use it in older patients. However, when applied for the appropriate indication, for the recommended duration of therapy, and with proper adjustments for renal function, reductions in drug-drug interactions and fall risk permit this therapy to be given safely in many cases. Patient education about bleeding risks and proper follow-up are essential.

Peripheral Arterial Disease

Etiology, Epidemiology, and Clinical Presentation in the Geriatric Population

Peripheral arterial disease (PAD) is a common form of atherosclerotic disease. PAD is often not diagnosed because it is frequently asymptomatic, especially in the elderly. PAD is associated with increased cardiovascular morbidity and mortality and is often thought to be an indicator of systemic atherosclerosis. The annual incidence of major cardiovascular events in patients with PAD is estimated to be 5% to 7% in patients.40

The prevalence of PAD increases with age. The Rotterdam Study evaluated the incidence of PAD and intermittent claudication (IC) in 10,275 patients in the Netherlands in the very elderly and the normal adult population. The incidences of PAD and IC in men between the ages of 55 and 59 years were 6.6% and 1%, respectively. For women between the ages of 55 and 59, the incidences of PAD and IC were 9.5% and 0.7%, respectively. In patients >85 years of age, the incidences of PAD and IC in men were 52% and 6.0%, respectively, and in women the incidences of PAD and IC were 59.6% and 2.5%.41

In 2001, the cost to Medicare of treating PAD was estimated at $4.37 billion dollars.42 This cost estimate did not include medications, durable medical equipment, or rehabilitation programs. In the Medicare population, 6.8% of patients received treatment for PAD in 2001. The proportion of the Medicare population undergoing treatment for PAD increased with age: 4.5% (65–74 years), 7.5% (75–84 years), and 11.8% (>85 years). Approximately 88% of costs were inpatient-related.42 These reported incidences are lower than those in other studies and suggest that earlier detection and prevention may help with inpatient costs associated with PAD in this population.
Patients between the ages of 50 and 69 with a history of smoking or diabetes and those older than 70 should undergo a review of vascular symptoms, including walking impairment and claudication symptoms. Exercise treadmill tests are sometimes used to evaluate functional limitation and response to therapy but may not be feasible in the elderly. Walking ability may be limited as a result of functional decline or co-morbid conditions, such as arthritis or pulmonary disease. The 6-minute walk test is an alternative.

**KEY POINT:** Appropriate evaluation of lower extremity fatigue and walking limitations should be performed in the elderly, because it is common to attribute these symptoms to the deconditioning of advancing age when the patient may, in fact, have PAD.

**Standard Adult Treatment Recommendations**

General treatment recommendations for adults can be found in the ACC/AHA Practice Guideline for Management of Peripheral Arterial Disease and the American College of Chest Physicians (ACCP) Guidelines on Antithrombotic Therapy for Peripheral Artery Occlusive Disease. Pharmacological treatment can be divided into two categories: antithrombotic therapy to prevent occlusion/reduce cardiovascular event rates and drug therapy for intermittent claudication symptoms. Aspirin 75–325 mg daily is recommended antithrombotic therapy with clopidogrel 75 mg daily as an acceptable alternative. Cilostazol is first-line therapy for patients who experience IC. Pentoxifylline can be used as a second-line agent for IC. PAD is a form of atherosclerotic disease, and risk reduction in the form of smoking cessation, glycemic control, hyperlipidemia management, and hypertension therapy should be emphasized.

The treatment guidelines do not generally make distinctions between the elderly and general adult population. Emphasis is placed on screening patients >70 years of age for PAD. Surgical interventions can also be helpful in patients with PAD who do not respond to pharmacotherapy and continue to experience significant impairment in daily life.

**Treatment Recommendations in the Geriatric Population**

Because the incidence of PAD is significantly higher in the older population, many of the studies included in the ACC/AHA and ACCP guidelines include patients older than 65; however, few studies include patients over the age of 80.

Treatment of PAD focuses on risk factor reduction. Risk reduction should continue to be a goal of treatment in geriatrics. PAD should be considered a clinical form of atherosclerotic disease and goals for risk factor management treated accordingly.

Antithrombotic therapy has been assessed in several trials that included patients with PAD. The Antithrombotic Trialists’ Collaboration was a large meta-analysis that helped form recommendations for PAD; however, data in elderly patients were not specifically available.

The CAPRIE trial compared the efficacy of clopidogrel 75 mg versus aspirin 325 mg in 19,185 patients with vascular disease. In the subgroup of patients with symptomatic PAD, the average age was 64.3 years. No patient exclusions were made based on age. Post hoc subgroup analyses of patients with PAD revealed a reduction of 23.8% in the relative risk of vascular events in the clopidogrel group. As no studies exclusively evaluate antithrombotic therapy in the geriatric population, treatment decisions are based on the assumption that the available data can be extrapolated to this population. As seen in other disease states, caution is required when making this assumption.

Exercise rehabilitation programs are recommended for all patients with symptoms of claudication. These programs should include 30–45 minutes of treadmill or track walking three times
per week for at least 12 weeks initially. Many of the studies evaluating such programs are small. The findings of a Cochrane database review that included 10 trials, 8 of which included patients >65 years of age, support the efficacy of exercise programs in patients with intermittent claudication. Another exercise trial that focused on the geriatric population (n = 61, mean age 70.5 years) reported a 134% increase in treadmill distance walked until the onset of claudication symptoms. The benefits of such programs have not been tested extensively in older persons, but most studies have been positive and, given the other health benefits of exercise, should be considered an option.

Cilostazol is currently the only recommended pharmacotherapy for symptoms of IC. The evidence in support of the efficacy of pentoxifylline is inconclusive, but this agent may be used as an alternative in patients who are intolerant of cilostazol. Most trials used to establish the efficacy of cilostazol did not exclude elderly patients, but the average age of participants was in the mid-60s.

Barriers to Treatment of the Geriatric Population

Bleeding risk must be considered in any patient receiving aspirin or clopidogrel therapy, but it is particularly important in elderly patients because of the higher risk. In the Clopidogrel in Unstable Angina to Prevent Recurrent Events (CURE) trial, the incidence of bleeding complications in the aspirin/placebo group increased with advancing age: 2.1% (<65 years), 3.1% (65–74 years), 3.6% (>75 years). The bleeding incidence was higher in patients in the aspirin and clopidogrel group: 2.5% (<65 years), 4.1% (65–74 years), 5.9% (>75 years). This antiplatelet combination is not currently recommended for the management of PAD. The geriatric population may experience a higher incidence of complications associated with GI bleeding than the younger population. Aspirin or clopidogrel should be used at the lowest dose proven effective, which is 81 mg and 75 mg, respectively, for the management of PAD. Symptoms of bleeding and complete blood counts should be monitored closely in the geriatric population to detect occult bleeding.

Declining kidney function must also be considered in pharmacotherapy for PAD. Kidney function must be monitored in patients on cilostazol therapy. If the serum creatinine is >2.5 mg/dL, concentrations of cilostazol and its active metabolites can be significantly increased and the drug should be used with caution. Pentoxifylline doses must be adjusted to 400 mg twice daily in patients with estimated CrCl 10–50 mL/min and to 400 mg once daily in patients with estimated CrCl <10 mL/min.

Heart failure is common in the geriatric population. Cilostazol should not be administered to patients with heart failure of any New York Heart Association (NYHA) classification, as other phosphodiesterase III inhibitors have been shown to decrease survival rates in patients with heart failure. Cilostazol undergoes a significant degree of metabolism by CYP450 3A4 enzymes. Elderly patients take a larger number of medications than younger patients, and the greater potential for drug interactions requires consideration. Cilostazol is an arterial vasodilator and can exacerbate hypotension and cause dizziness. Geriatric patients must be screened for orthostasis and hypotension prior to initiating therapy with cilostazol, as these conditions are often more common in this population.

Heart Failure

Etiology, Epidemiology, and Clinical Presentation in the Geriatric Population

The incidence of heart failure increases with age. According to national statistics from the AHA/American Stroke Association, the incidence of heart failure is 9.3% in men and 4.8% in women between the ages of 60–79 years. In patients ≥80 years of age, the incidence increases to 13.8% in men and 12.2% in women. In 2009, heart failure is estimated to cost the United States $37.2
billion.\textsuperscript{21} It is also the most common discharge diagnosis for patients 65 years and older. The incidence of mortality associated with heart failure is also higher in the geriatric population. Concomitant disease states that contribute to development of heart failure or precipitate heart failure, including hypertension, atrial fibrillation, coronary artery disease, and diabetes mellitus are also more common in the elderly.

Changes in anatomy and physiology of the cardiovascular system contribute to the incidence of heart failure in older patients, including increased vascular stiffness and decreased endothelial function, which increases ventricular afterload.\textsuperscript{48} In older adults, diminished response to beta-adrenergic stimulation occurs due to decreased receptor density and sensitivity. Elderly patients have higher plasma concentrations of catecholamines but are less responsive to circulating catecholamines.\textsuperscript{54} Left ventricular (systolic) function is often preserved and normal in older patients, but diastolic function is often impaired. This type of heart failure is sometimes referred to as \textit{diastolic dysfunction}, but this is not an official term. The incidence of heart failure with preserved \textit{left ventricular function} is high in the geriatric population, especially in women. The Cardiovascular Health Study evaluated heart failure in community-dwelling older adults (average age 79 years) and found that 55% of these patients with heart failure had preserved left ventricular function.\textsuperscript{55} Management strategies are different for patients with heart failure and preserved left ventricular function, and distinguishing the presence of this type of heart failure is important in the elderly.

\textbf{KEY POINT:} Diagnosis and clinical presentation of heart failure can be more complicated in older patients. Chronic deconditioning can mimic heart failure symptoms. Chronic lung disease can mimic shortness of breath and rales heard on auscultation. Peripheral edema can be caused by venous insufficiency and medications such as calcium channel blockers and nonsteroidal anti-inflammatory drugs (NSAIDs). Atypical presentation of heart failure also occurs in the elderly, with such symptoms as anorexia, confusion, generalized weakness, and fatigue. Subjective complaints can render diagnosis of heart failure difficult, and echocardiography should be used as an objective measure to determine left ventricular function. The use of B-type natriuretic peptide (BNP) for diagnosis and monitoring of treatment in elderly patients can be complicated, as plasma BNP concentrations tend to be higher in the elderly, and interpretation of normal concentrations with the different assays can be difficult.\textsuperscript{54-57} More trials are needed to determine the role of BNP monitoring in the elderly.

\textbf{Standard Adult Treatment Recommendations}

Heart failure management for adults is described in the 2013 ACCF/AHA Heart Failure Guidelines and the Heart Failure Society of America (HFSA) 2010 guidelines.\textsuperscript{58,59} The mainstays of pharmacologic therapy continue to be ACE inhibitors or ARBs, beta blockers (carvedilol, bisoprolol, extended-release metoprolol), diuretics, aldosterone antagonists, digoxin, and hydralazine/nitrate combination for African American patients. In the ACCF/AHA guidelines, patients are categorized into Stages A–D based on the progression of heart failure. One of the aims of this classification is to identify those at risk for preventative measures. The NYHA classification system categorizes patients who have already developed heart failure into class I–IV based on symptoms and functional status. Appropriate pharmacological treatment depends on the staging of heart failure.
Treatment Recommendations in the Geriatric Population

Several of the trials used in the national guidelines included patients over the age of 65 years. However, many of these trials only included a small percentage of patients over 80 years of age, and some included no patients older than 80. The HFSA guidelines include a small subsection regarding treatment of elderly patients. The primary specification regarding pharmacotherapy in elderly patients is to use ACE inhibitors and beta blockers in the absence of contraindications in those over 80. The strength of this recommendation in the older population is based on cohort and case-control studies, while in the very old (over 80) it is based simply on expert opinion.

A review of the literature reveals some studies of the pharmacotherapy of heart failure in patients over 80. Many of these studies are post hoc analyses of major trials or meta-analyses of several smaller studies. The evidence in major drug classes is discussed below. Efficacy of diuretic therapy in heart failure is not specifically addressed, but these agents are usually effective in older patients. There are also limited data regarding the efficacy of hydralazine/nitrate and aldosterone antagonist therapy in the elderly.

Beta Blockers

The Study of the Effects of Nebivolol Intervention on Outcomes and Rehospitalisation in Seniors with Heart Failure (SENIORS) was a randomized, placebo-controlled trial that evaluated a alpha-1 selective blocker, nebivolol, in patients ≥70 years with heart failure, regardless of left ventricular ejection fraction. The mean age of participants was 76 years in both groups. The primary outcome was all-cause mortality or cardiovascular hospital admission (time to first event). Significantly fewer patients in the nebivolol group reached the primary outcome (p = 0.039); differences in efficacy between the groups became apparent at 6 months of therapy. No difference was found in cardiovascular hospital admissions, and, based on subgroup analyses in the age groups 75–85 years versus those >85 years, age was not found to be a significant influence on primary outcome. This study did not allow patients with significant kidney disease or hepatic dysfunction to enroll, which may limit the generalization of the results to the entire elderly population.

A subgroup analysis of the Metoprolol CR/XL Randomized Intervention in Heart Failure (MERIT-HF) study evaluated the efficacy and tolerability of metoprolol XL in patients ≥65 years (average age 72). The analysis found that there were significant reductions in all-cause mortality (37%), sudden death (43%), and hospitalization (36%) associated with metoprolol XL compared with placebo in this elderly population. The analysis also showed significant benefit specifically for patients over 75. However, in patients 65 or older there was a significantly larger proportion who discontinued therapy. In addition, older patients achieved a lower dose than younger patients (146 mg versus 168 mg). Furthermore, there were significantly fewer older patients taking ACE inhibitors, and a larger proportion of older patients with atrial fibrillation or past MIs. This analysis is limited in that it was performed post hoc, and that the trial was not originally designed to determine differences in efficacy in elderly patients. The Carvedilol Open Label Assessment (COLA) II study evaluated the tolerability of carvedilol in patients ≥70 years, and demonstrated that 80% of patients achieved a specified carvedilol dose and maintained therapy for at least 3 months. As evidenced by these two larger studies, beta blockers appear to decrease mortality and hospitalization and are as well tolerated in elderly patients as in younger. Beta blockers should be recommended for use in elderly patients with heart failure.

ACE Inhibitors

No large placebo-controlled trials have analyzed the efficacy of ACE inhibitor therapy specifically in the elderly with heart failure. Several landmark trials included patients over 65; however, there is not as much evidence in the very old. In one study, patients in nursing homes who were on ACE inhibitors or digoxin were evaluated retrospectively. The average age of patients in the
ACE inhibitor group was 84, whereas the average age in the digoxin group was 85. Outcomes assessed were overall mortality, hospital admissions, and rate of functional decline. Compared with the digoxin group, there was a significant reduction in the relative risk of mortality (0.89, 95% CI 0.83–0.95) in the ACE inhibitor group. There was only a nonsignificant trend toward a reduced incidence in hospitalization, but there was a significant reduction in the rate of physical decline in patients taking ACE inhibitors. This evaluation did not distinguish between heart failure with or without preserved left ventricular function, and no consideration was given to doses or previous therapies.

A systematic overview of the efficacy of ACE inhibitors in five large trials was conducted and included 12,763 patients. The analysis found that the incidence of mortality was lower (23% versus 26.8%) in patients taking ACE inhibitors compared with those not receiving it. In addition, the incidence of readmission for heart failure was lower in the ACE inhibitor group (13.7% versus 18.9%). The mean age of patients in this analysis was 61. In a subgroup analysis of specific age groups, there was a smaller mortality benefit in patients older than 75. Three of the major trials included only post-MI patients. Despite no overwhelming evidence specifically in elderly patients, ACE inhibitors should be used in the elderly population with heart failure, if tolerated. The benefits of ARBs have been demonstrated to be comparable to that of ACE inhibitors in younger patients with heart failure. ARBs may be tried in elderly patients who do not tolerate ACE inhibitors.

Digoxin

In the Digoxin Investigation Group (DIG) study, patients with heart failure were randomized in double-blind fashion to receive therapy with digoxin or placebo. They were stratified by age, and the outcomes assessed were mortality, hospitalizations for heart failure, hospitalizations for digoxin toxicity, and withdrawal of digoxin therapy. The study included 2,092 patients between 70 and 79 and 425 patients 80 and older. The analysis found that the incidence of hospitalizations due to heart failure was reduced and independent of age. However, age was a significant predictor of hospitalization for digoxin toxicity and withdrawal. Digoxin did not reduce the incidence of mortality. It should only be used in elderly patients with left ventricular systolic dysfunction who remain symptomatic despite maximally tolerated doses of a beta blocker, ACE inhibitor, and diuretic. Some studies have demonstrated a lower target range for serum digoxin concentrations of 0.5–0.8 ng/mL that provides as much benefit for heart failure management as higher serum concentrations. This lower therapeutic serum concentration is acceptable in older patients, especially in view of their increased risk of digoxin toxicity. The Beers Criteria does not recommend going above doses of 0.125 mg daily in heart failure, to lessen the risk for toxicity in the elderly.

Combination Therapy

The Trial of Intensified versus standard Medical Therapy in Elderly Patients with Congestive Heart Failure (TIME-CHF) was conducted to determine whether intensive management is more effective than standard medical therapy. The study enrolled 499 patients with a mean age of 82 in the very old age group and 69 in the younger group. It compared therapy guided by plasma BNP concentrations with symptom-guided therapy. The primary outcomes were hospitalization-free survival and quality-of-life measures at 18 months. There was no significant difference in the primary outcomes between the BNP-guided and symptom-guided groups. The BNP-guided group achieved higher doses of ACE inhibitors and beta blockers and was regarded as the more aggressive treatment group. When the patients were stratified into age groups of 60–74 and ≥75, it was found that the younger group may benefit more from the BNP-guided therapy. In the group that was ≥75, benefit from BNP-guided therapy was not apparent, and, in fact, this treatment strategy was potentially harmful. This trial suggests that increasing drug doses aggressively may not benefit patients with heart failure that are ≥75. These findings warrant further investigation.
KEY POINT: Therapy with beta blockers and ACE inhibitors should be attempted in elderly patients with heart failure, unless there are contraindications. Lower starting doses and slower dose titration may be necessary to maximize safety and tolerability.

Barriers to Treatment of the Geriatric Population

Proper diagnosis of heart failure can be a barrier to proper treatment, because the symptoms can mimic other common disease in the elderly. In addition, hesitation to attempt titration of heart failure medications due to risk for adverse effects can also be a barrier to proper treatment. Titration of doses of medications for heart failure management can be more difficult in elderly patients. For each class of medications, there are specific issues relative to the elderly. When initiating therapy with beta blockers, the lowest dose should be used. Starting doses for the three beta blockers with proven efficacy in heart failure are metoprolol XL 12.5–25 mg once daily, bisoprolol 1.25 mg twice daily, and carvedilol 3.125 mg twice daily. Heart failure symptoms should be stable before initiation of therapy, and doses should be increased every 2–4 weeks to target or to the maximally tolerated dose. Therapy with ACE inhibitors/ARBs should also be initiated at the lowest dose possible and titrated every 1–2 weeks. Hypotension and bradycardia can limit the ability to titrate the dose in the elderly. Carvedilol may be associated with a slightly higher risk of hypotension than other beta blockers, due to its beta-blocking properties. Staggering the time of administration of doses of medications that can lower blood pressure and eliminating other anti-hypertensive agents are strategies that can be used to reduce risk and increase tolerability.

Hyperkalemia is a concern with the use of ACE inhibitors/ARBs and aldosterone antagonists. The Beers Criteria recommends limiting doses of spironolactone to 25 mg daily due to risk of hyperkalemia in the elderly. CKD in elderly patients further increases the risk. Careful monitoring of serum creatinine and potassium concentrations, particularly in elderly patients, is necessary with each dose increase.

Elderly patients may be more sensitive to volume depletion associated with diuretics, and kidney disease may reduce diuretic efficacy in some patients. Thiazide diuretics are not useful for patients with estimated CrCl <30 mL/min; therefore, loop diuretics are needed. Hypotension and kidney function should be monitored carefully in these patients. Potassium loss can be a concern with loop diuretics, especially in patients taking digoxin. Hyperkalemia can increase the sensitivity of cardiac tissue to effects of digoxin and increase the risk of digoxin toxicity. Monitoring of serum potassium concentrations should be performed on a regular basis.

The half-life of digoxin is increased significantly in patients with kidney disease. The usual is 30–40 hours, but in patients with kidney disease the half-life can be as long as 4–6 days. Dose adjustment can be performed by altering the dosing interval or decreasing the maintenance dose. The following are suggested adjustments based on dosing interval or total daily dose:

- For patients with estimated CrCl >50 mL/min, administer every 24 hours
- For patients with estimated CrCl 10–50 mL/min, administer every 36 hours or give 25% to 75% of the usual dose
- For patients with estimated CrCl <10 mL/min, administer every 48 hours or give 10% to 25% of the usual dose
- Decreased skeletal muscle mass or volume depletion in the elderly reduces the volume of distribution of digoxin and increases the risk of toxicity.

Polypharmacy increases the risk of drug interactions and can contribute to higher toxicity risk. All patients with heart failure should also be counseled regarding avoidance of nonprescription NSAIDs. Elderly patients may be more likely
to use these medications as a result of comorbid disease states such as osteoarthritis. Acetaminophen should be recommended in lieu of NSAIDs.

A few recent studies have demonstrated a possible link between heart failure and cognitive impairment or dementia. Proposed mechanisms include decreased cerebral blood flow, leading to further ischemia and possibly degeneration of neurons. Further analyses are needed, but it is reasonable to perform cognitive screening in elderly patients with heart failure.

**Atrial Fibrillation**

**Etiology, Epidemiology, and Clinical Presentation in Geriatric Population**

The prevalence of atrial fibrillation increases with aging. Atrial fibrillation is present in approximately 0.5% of patients between 50 and 59; in individuals >65, the prevalence is roughly 5% and rises to 8% and 10% in patients >80 years. The incidence of atrial fibrillation is <0.1% per year in individuals under 40 but increases to 1.5% and 2.0% per year in women and men, respectively, over 80.

Atrial fibrillation is associated with a two-fold increase in the incidence of cardiovascular mortality. It increases the risk for ischemic stroke fivefold and is responsible for approximately 15% of all strokes in the United States. Atrial fibrillation may be responsible for as many as 24% of all strokes in individuals between 80 and 89.

Risk factors for atrial fibrillation include hypertension, coronary artery disease, heart failure, valvular heart disease, and rheumatic heart disease. The common feature of these conditions is the development of left atrial hypertrophy, which leads to derangements in atrial impulse conduction and refactoriness. Hyperthyroidism is a potentially correctable cause of atrial fibrillation. This arrhythmia may occur following thoracic surgery, including coronary artery bypass graft surgery, pulmonary resection, or esophagectomy. In these situations, the arrhythmia is usually transient, lasting only a few days. Drug-induced atrial fibrillation is uncommon but has been reported in association with binge drinking of alcohol (the so-called “holiday heart” syndrome). In addition, bisphosphonate drugs have recently been associated with inducing new cases of serious atrial fibrillation; this is particularly pertinent to the elderly population, as many elderly patients with osteoporosis take these drugs for prevention of fractures. The association between bisphosphonate drugs and new-onset serious atrial fibrillation is not certain and requires further study.

Atrial fibrillation appears on the ECG as an irregularly irregular rhythm with no visible P waves, but rather an undulating baseline, representing chaotic atrial electrical activity. Ventricular rates during atrial fibrillation generally range from 100 to 180 beats per minute. Symptoms associated with atrial fibrillation are typically dependent on the ventricular rate and include palpitations, dizziness, lightheadedness, near-syncope, syncope, shortness of breath, and, in patients with underlying coronary artery disease, angina. Elderly patients have atypical presentations or may be asymptomatic. An evaluation of pulse may reveal irregular heart rate in an otherwise asymptomatic individual. In some patients, the first symptom of atrial fibrillation is a stroke. Depending on the degree to which cardiac output is compromised, patients may become hypotensive and hemodynamically unstable.

**Standard Adult Treatment Recommendations**

Treatment recommendations are provided in the 2013 ACC/AHA Task Force on Practice Guidelines Report: Management of Patient with Atrial Fibrillation and the 2012 American College of Chest Physicians Evidence-Based Clinical Practice Guidelines: Antithrombotic Therapy for Atrial Fibrillation. The primary goals of therapy include ventricular rate control, conversion to sinus rhythm, reduction in the frequency of episodes (for patients with paroxysmal atrial fibrillation), and stroke prevention.
Ventricular Rate Control

Diltiazem, verapamil, and a beta blocker are first-line agents for controlling ventricular rate. If those medications are contraindicated for rate control, digoxin or amiodarone is recommended. The 2012 Beers Criteria supports this by stating antiarrhythmics should not be used first-line for atrial fibrillation. The goal of therapy is reduction in ventricular rate to <100 BPM or, if that cannot be achieved, reduction in ventricular rate >20% from the pretreatment value with alleviation of patient symptoms.

Conversion to Sinus Rhythm

Conversion of atrial fibrillation to sinus rhythm is safe in patients in whom the episode of atrial fibrillation has persisted for <48 hours. However, if the patient's episode of atrial fibrillation has persisted ≥48 hours or if the duration is unknown, conversion to sinus rhythm with direct current cardioversion (DCC) or drugs may be dangerous because after 48 hours the possibility exists that a clot may have formed in the left atrium. The process of converting atrial fibrillation to sinus rhythm may dislodge the clot and cause a stroke. Therefore, in many institutions a transesophageal echocardiogram (TEE) is performed in patients with atrial fibrillation ≥48 hours or of unknown duration. If a left atrial clot is detected by TEE, conversion to sinus rhythm is deferred, and anticoagulation is initiated for at least 4 weeks. However, if no left atrial clot is detected by TEE, sinus rhythm may be restored.

Although there are no comparative trials of DCC versus drug therapy, DCC is generally believed to be more effective. Pharmacological conversion of atrial fibrillation to sinus rhythm may be achieved with dofetilide, ibutilide, amiodarone, propafenone, or flecainide, and the exact agent is selected according to presence of contraindications.

Reduction in the Frequency of Episodes of Atrial Fibrillation

This goal of therapy is commonly expressed as maintenance of sinus rhythm. Several randomized studies have compared rate-control and rhythm-control strategies and found no advantage to rhythm-control therapy with respect to mortality or stroke. However, some data generated in these studies suggested that there may be trends toward worse outcomes, including mortality, associated with rhythm control strategies, presumably as a result of proarrhythmic effects of the drugs. Therefore, drug therapy for reduction of frequency of episodes should be reserved for patients with paroxysmal atrial fibrillation who continue to experience symptoms despite optimal doses of drugs for ventricular rate control.

Propafenone, flecainide, amiodarone, sotalol, or dofetilide are potential choices for maintenance of sinus rhythm; however, propafenone and flecainide are contraindicated in patients with left ventricular dysfunction. Amiodarone has been shown to be more effective than sotalol, is rarely associated with the proarrhythmia known as torsades de pointes, and, therefore, is a preferred drug by many clinicians; however, amiodarone is associated with a long list of noncardiovascular adverse effects, including pulmonary fibrosis, thyroid dysfunction, hepatotoxicity, photosensitivity, blue-grey skin discoloration, corneal microdeposits, and others.

Stroke Prevention

The CHADS2 score is a tool that helps to estimate stroke risk in patients with atrial fibrillation. The CHADS2 scoring is shown in Table 7-3. The CHA2DS2-VASC scoring tool also may be considered when establishing stroke risk. This tool was not included in some of the current guidelines and no guidelines currently recommend it over the CHADS2 score; however, CHA2DS2-VASC does take into account gender, presence of vascular disease, and risk in the 65–74-year age group. CHA2DS2-VASC may be considered in those with a low CHADS2 score of 0–1 to help further assess risk. A summary of ACCP recommendations for stroke prevention in the general adult population can be found in Table 7-2.

These recommendations are typically based on the CHADS2 score of an individual patient. Aspirin, warfarin, dabigatran, rivaroxaban, and
Apixaban may all be alternatives given the patient’s risk and individual patient factors, as shown in Table 7-2, for nonvalvular atrial fibrillation. For patients with valve disease or prosthetic heart valves, warfarin is the anticoagulant of choice for stroke prevention.78

### Treatment Recommendations in Geriatric Population

Treatment recommendations for ventricular rate control, conversion of atrial fibrillation to sinus rhythm, and reduction of the frequency of episodes for patients with paroxysmal atrial fibrillation are the same in elderly as in younger patients. Age does play a factor in stroke prevention.78,79 Based on the ACCP guidelines, patients at intermediate risk for stroke (i.e., a CHADS2 score of 1) should be on oral anticoagulation.78 Age 75 years and over alone would create a CHADS2 score of 1. For patients in this group who choose not to take oral anticoagulation, recommend clopidogrel 75 mg with aspirin.78

Dabigatran, rivaroxaban, and apixaban are also approved for stroke prevention in nonval-
vular atrial fibrillation; they are acceptable alternatives to warfarin. However, these newer agents have not been studied as extensively in the elderly. The efficacy and some of the safety issues with these newer anticoagulants is discussed further in this section.

The Randomized Evaluation of Long-Term Anticoagulation Therapy (RE-LY) trial looked at dabigatran use in nonvalvular atrial fibrillation in over 18,000 patients. The average age in this trial was 71, and the follow-up was approximately 2 years. The interventions were warfarin versus dabigatran 110 mg twice daily or dabigatran 150 mg twice daily. The trial showed noninferiority of dabigatran 150 mg twice daily with warfarin and was given FDA approval for this indication. The primary outcome was stroke or systemic embolism. The reduction was consistent across all CHADS$_2$ categories. In subgroup analyses of bleeding, age over 75 years and CrCl <30 mL/min were risk factors: an increase of as much as 20%. These data led to the inclusion of dabigatran on the Beers Criteria.

The Rivaroxaban Versus Warfarin in Nonvalvular Atrial Fibrillation (ROCKET AF) trial compared rivaroxaban to warfarin in more than 14,000 patients. The primary outcome was again stroke or systemic embolism, and follow-up was 2 years. The average age of patients in this trial was 73. This trial showed noninferiority of rivaroxaban to warfarin. The safety outcomes included major bleeding such as intracranial hemorrhage. There was no significant difference between the two groups. The Apixaban Versus Warfarin Patient with Atrial Fibrillation (ARISTOTLE) trial enrolled more than 18,000 patients and had a mean follow-up of 1.8 years. The average age of patients in this trial was 70. The primary outcome was also stroke or systemic embolism. Apixaban was shown to be noninferior to warfarin. There was a trend toward less bleeding with apixaban.

All three of these new agents are FDA approved for use in the geriatric population, and the ages and CHADS$_2$ scores in the major trials of these agents included various subgroups of geriatrics. Efficacy was established in some subgroups; however, there are several barriers that may limit use of these agents in specific patients. One of the major drawbacks of each of these new anticoagulants versus warfarin is the lack of an antidote to bleeding. Clearance of these agents may be longer in geriatrics, leading to longer recovery when a patient is bleeding, or if an emergent surgery is needed. Further discussion of the specific subgroups in which these newer anticoagulants may be problematic is discussed in the next section.

**Barriers to Treatment in the Geriatric Population**

Elderly patients are at greater risk for adverse effects associated with some of the antiarrhythmic agents used for the management of atrial fibrillation. For example, elderly patients are more likely to experience constipation associated with verapamil or diltiazem. In addition, drugs such as sotalol, ibutilide, and dofetilide are associated with the risk of the potentially life-threatening ventricular arrhythmia known as torsades de pointes; elderly patients are at greater risk of experiencing this drug-induced proarrhythmia. Furthermore, as a result of declining kidney function elderly patients may be at higher risk of experiencing elevated serum digoxin concentrations and associated digoxin toxicity. A number of the adverse effects associated with amiodarone occur with increased frequency in elderly patients, including sinus bradycardia, hypothyroidism, pulmonary fibrosis, and neurologic adverse effects such as ataxia, tremor, peripheral neuropathy, insomnia, and impaired memory. As a result of these considerations, digoxin (at doses >0.125 mg daily) and amiodarone, dofetilide, dronedarone, flecainide, ibutilide, procainamide, propafenone, quinidine, and sotalol first-line for atrial fibrillation are included in the Beers Criteria for potentially inappropriate drug use in older adults.

There are numerous considerations for the use of warfarin and some of the newer anticoagulants in elderly patients, which are discussed here and in the Venous Thromboembolism section of this chapter.
**Warfarin**

Conflicting data exist regarding whether elderly patients are at increased risk of bleeding complications associated with warfarin therapy. However, it is well established that the risk of warfarin-induced bleeding is increased in the very old population (patients >80). Warfarin therapy is not contraindicated in this population, but careful monitoring of international normalized ratio (INR) and signs and symptoms of bleeding is warranted. In addition, many elderly patients are at risk of falls; in patients with a history of falls, or who appear to be at risk of falling, careful assessment of the risks and benefits of warfarin therapy is often performed. Conventional thinking has been that if a therapeutically anticoagulated patient falls and hits his or her head, an intracranial hemorrhage may result, which may be as catastrophic as a thromboembolic stroke. In the frail elderly population who are at risk of falling, aspirin is often substituted for warfarin because of the risk of intracranial hemorrhage.

However, evidence suggests that the risk of a patient falling and experiencing a significant cerebral bleed during warfarin therapy is low. Man-Son-Hing et al.\(^8^4\) utilized a Markov decision model incorporating previously published literature regarding the risk of accidental fall and cerebral bleeding during warfarin therapy in patients 65 or older. The authors concluded that warfarin therapy was associated with a larger number of quality-adjusted life-years than aspirin therapy or no antithrombotic therapy (12.90 versus 11.17 versus 10.15, respectively). In addition, the authors concluded that, based on sensitivity analysis, the risk of falling was not an important determining factor of optimal antithrombotic therapy. Therefore, perceived risk of falling may not be a sufficiently important factor to discourage warfarin administration for stroke prevention in elderly patients with atrial fibrillation.

Because elderly patients are usually taking a substantially larger number of medications than younger patients, there is a greater potential for drug interactions associated with warfarin that could increase the risk of supratherapeutic INR and bleeding. Careful assessment of concomitant drug therapy, particularly drugs that inhibit the function of CYP450 2C9, and appropriate adjustment of warfarin dose, if needed, is important in the elderly population. This is often especially problematic with antibiotic drugs, as these are usually prescribed on an acute, short-term basis. Routine warfarin monitoring schedules cannot always capture INR excursions caused by interaction as antibiotic prescribing will not often coincide with a predictable schedule, so the ability to identify a drug interaction is dependent on prospective drug regimen review by the prescriber and pharmacist at the time of antibiotic initiation.

There are several tools that attempt to estimate bleeding risk in patients. The Outpatient Bleeding Risk Index (OBRI) takes into account four risk factors: (1) age \(\geq 65\) years, (2) history of stroke, (3) history of GI bleeding, and (4) one or more of the following: recent MI, hematocrit <30%, serum creatinine >1.5 mg/dL, and diabetes mellitus. Each of these four categories counts as 1 point. Those scoring 0 are at low risk, 1–2 are at intermediate risk, and \(\geq 3\) at high risk. The corresponding risks of major bleeding at 48 months were 3%, 12%, and 53%.\(^8^5\) The HAS-BLED score has been used to determine bleeding risk in atrial fibrillation patients. There are 9 points that can be given: hypertension, abnormal liver function, abnormal kidney function, stroke, bleeding tendency, labile INRs, elderly (age >65), alcohol abuse, and drugs (taking aspirin or NSAIDs). If a patient scores 0 points that corresponds to 1.13 bleeds per 100 patient years; 1 point is 1.02 bleeds, 2 points is 1.88 bleeds, 3 points is 3.74 bleeds, and 4 points is 8.70 bleeds. There are no data to support estimation of bleeds for scores of 5–9.\(^8^6\) Both of these tools can be used to help determine whether the risk of bleeding in elderly patients outweighs the risk of stroke of thromboembolism.

**Dabigatran**

As discussed above, the bleeding risk with dabigatran is likely higher in those 75 years and older and those with CrCl <30 mL/min. Also, there are administration issues to consider when using dabigatran in the geriatric population. The
capsules cannot be opened and sprinkled on food, restricting use of this medication to those who do not have swallowing issues. They must be kept in their original bottle and cannot be placed in a medication organizer. The elderly tend to have complex regimens in which an organizer is needed; adherence to dabigatran therapy might be affected if the medicine must be omitted from organizers. In addition, dabigatran is metabolized by p-glycoprotein; therefore, interaction with p-glycoprotein must be taken into account. Agents specifically listed for dose adjustment include dronedarone and oral ketoconazole.

**KEY POINT:** The newer anticoagulants may be used in some geriatric patients after careful evaluation of the drugs’ safety in each individual patient. Extra attention should be paid to renal function, significant drug interactions, medication adherence history, need for immediate procedures, insurance coverage, and bleeding risk when considering initiating these new agents.

**Rivaroxaban**

Rivaroxaban is metabolized by CPY3A4, and drug interactions need to be taken into account when deciding whether this agent should be used. There are also dose limitations with renal function. If CrCl is 15–50 mL/min, a reduced dose of rivaroxaban should be used. If CrCl is <15 mL/min, the medication should not be used. There is slightly different renal dosing for the indication of venous thromboembolism discussed in that section.

**Apixaban**

This medication is metabolized by CYP3A4 as well. Drug interactions must be taken into account when deciding whether to initiate this agent. There are recommendations regarding when to reduce the dose of apixaban that are not based completely on renal function. Systemic exposure seems to be increased with age, separate from renal function. If a patient has a serum creatinine of 1.5 mg/dL or higher and has one of the following: age ≥80 years or body weight ≤60 kg, a reduced dose of apixaban should be used. It is also recommended if CrCl is <25 mL/min, apixaban should be avoided.

Cost is also a consideration with the new anticoagulants. The price of these medications is significantly higher than warfarin; however, there is less cost for monitoring. The copays may be higher and prior authorizations required for use of these agents for those on Medicare Part D plans. Patients should also be prepared to encounter the “doughnut hole” gap in coverage with many Medicare Part D plans faster due to the cost of these medications.

**STROKE**

**Etiology, Epidemiology, and Clinical Presentation in the Geriatric Population**

Stroke is a significant cause of morbidity, and is the third leading cause of death in the United States. The risk of stroke doubles every 10 years after the age of 55. The cost of stroke care is high because many patients have residual effects, and it was estimated to be $68.9 billion in 2009.

The incidence of mortality associated with stroke rises with age, demonstrating a need for prevention and education in the geriatric population. Median survival after a first stroke in patients age 60–69 is 6.8 years for men and 7.4 years for women. In patients 80 and older, median survival is 1.8 years for men and 3.1 years for women. As many as 26% of patients receive institutionalized care after stroke. Risk factors for stroke, such as hypertension and atrial fibrillation, also are more prevalent in geriatrics.

Ischemic stroke accounts for approximately 87% of cases, whereas hemorrhagic stroke accounts for the remaining 13%. This ratio takes into account all age groups and is representative of the older population. Clinical presentation does not differ greatly in the geriatric population.
Co-morbid disease states, such as dementia, may make recognition of stroke symptoms more difficult. Patients and caregivers require significant education about recognizing stroke, because the timing of treatment following onset is an important factor in determining outcome.

**Standard Adult Treatment Recommendations**

The standard of care for stroke is discussed in the AHA/ASA guidelines and the 2012 ACCP guidelines on stroke.90,91

The source (hemorrhagic, noncardio-embolic, cardioembolic) and time of onset of symptoms are important factors in treatment. Thrombolytic therapy should only be used if the presentation is within 3 hours of onset and the etiology of the stroke is ischemic. The only FDA-approved thrombolytic drug for management of ischemic stroke in the United States is tissue plasminogen activator (t-PA), and patients must be evaluated for inclusion and exclusion criteria for its use. The source of the stroke affects whether antiplatelet or anticoagulant treatment is administered for secondary prevention. Cardioembolic strokes should be prevented with warfarin. Noncardioembolic strokes should be prevented with aspirin, clopidogrel, or aspirin–extended-release dipyridamole.

The optimal antiplatelet medication for secondary prevention of stroke is not completely clear. Aspirin, extended-release dipyridamole with aspirin, and clopidogrel all are acceptable choices per guidelines. The AHA/ASA guidelines have suggested that extended-release dipyridamole with aspirin may be a better choice based on the European/Australian Stroke Prevention in Reversible Ischaemia Trial (ESPRIT) and other previous trials.92 Since publication of the AHA/ASA guidelines, the Prevention Regimen For Effectively Avoiding Second Strokes (PROFESS) trial has been published, in which the efficacy of clopidogrel was compared with that of extended-release dipyridamole combined with aspirin for secondary prevention of stroke.93 In this study, the efficacy of both treatment strategies on stroke recurrence was similar. All these therapies remain first-line options, although cost is a significant factor, as aspirin therapy costs much less than the other two therapeutic strategies. Future studies are required to determine whether there is a clear benefit with any of the specific treatments.

Ticlopidine is an alternative agent for patients who cannot tolerate other antiplatelets. Use of ticlopidine is quite limited due to adverse effects, including bone marrow suppression, diarrhea, and aplastic anemia. Transient ischemic attack should be considered reason for secondary prevention.

The Management of Atherosclerosis with Clopidogrel in High-Risk Patients (MATCH) trial evaluated the efficacy of the addition of aspirin therapy to clopidogrel for reducing the incidence of vascular events, including stroke.94 This trial included patients with a history of stroke within the previous 3 months plus additional risk factors for vascular events. All patients received clopidogrel 75 mg daily and were randomized to receive either aspirin 75 mg daily or placebo. The study found no significant decrease in vascular events with the combination of aspirin and clopidogrel compared with clopidogrel alone. However, there was a significantly higher incidence of life-threatening bleeding in patients treated with the combination of aspirin and clopidogrel. Therefore, combination therapy with clopidogrel and aspirin is not recommended for secondary prevention of stroke.

**Treatment Recommendations in the Geriatric Population**

The majority of the trials used in development of the national guidelines for stroke included patients over age 65, most with a mean age in the 60s. The guidelines are applicable to most geriatric patients, with special considerations discussed in this section. However, the subgroup of patients over 80 was not as well represented in this evidence base.

The National Institute of Neurological Disorders and Stroke (NINDS) study of the ef-
cacy of tissue plasminogen activator for ischemic stroke enrolled patients with mean age of 67 ± 10 years. There have been several follow-up studies specifically in patients over 80. In general, these studies have shown that thrombolytic therapy should not be withheld in patients with stroke who are ≥80 years, if other criteria for receiving the medication are met. Although some trials showed that a higher proportion of younger patients achieved a favorable outcome associated with thrombolytic therapy than in patients ≥80 years, there was still benefit reported in the very elderly. The lower proportion of patients ≥80 years who benefitted from thrombolytic agents may be partially explained by the larger number of comorbid conditions in the very old, and the fact that they experienced more severe strokes in some trials. Several of the studies were retrospective reviews or post hoc analyses of data and must be interpreted in that context. However, there is much evidence that age should not be an automatic exclusion to thrombolytic therapy.

The Chinese Acute Stroke Trial (CAST) and the International Stroke Trial (IST) were major studies that established the benefit of early aspirin therapy in patients with ischemic stroke, and their data are applicable to the geriatric population who cannot receive thrombolytic therapy. In the CAST trial, 28% of patients were over 70, whereas 26% of patients enrolled in the IST trial were ≥80 years of age.

Several of the landmark trials of secondary prevention of stroke included patients over 65, and secondary prevention recommendations should be applied to all age groups. The Anti-thrombotic Trialists’ Collaboration investigated the efficacy of antiplatelet therapy in patients over age 65 and reported that this group derives benefits similar to younger patients. Some studies have shown lower rates of appropriate anticoagulation or antiplatelet therapy after stroke in the geriatric population, and it should be emphasized that the use of these agents for secondary prevention should be advocated in elderly patients, as this is often the highest risk group. The role of primary prevention in the geriatric population, especially the very old, is not as clear, as there are few data. If a patient’s 10-year risk for coronary heart disease is >10%, primary prevention should be considered. Future trials should provide more guidance.

Hormone replacement therapy for older women has been found to increase the risk of stroke and should be avoided or used for the shortest duration possible. Post-stroke depression, dementia, and the development of seizures are common, as is dysphagia (discussed in Chapter 10), functional decline associated with loss of mobility or contractures, and somnolence. Antidepressants, cholinesterase inhibitors, memantine, antiepileptics, nutritional supplements, appetite stimulants, muscle relaxants, and psychomotor stimulants are often added to a patient’s regimen as interventions for these problems. In such instances, critical evaluation of patient outcomes is necessary, as this is often a source of polypharmacy-related problems.

**Barriers to Treatment in the Geriatric Population**

A potential barrier to early presentation of stroke in geriatrics is transportation to the emergency department. It should be stressed that patients must call 911 immediately if stroke symptoms occur.

**KEY POINT:** Patients and caregivers should be educated to recognize the symptoms of stroke, allowing them to get to the emergency department sooner.

There is a risk of bleeding in association with any of the above medications used for acute treatment or prevention. Some evidence shows small increases in bleeding risk associated with these agents as age increases, but there is also evidence to the contrary. The risks and benefits of therapy in each patient must be weighed. Factors such as frailty, falls, previous GI bleed, peptic ulcer disease, polypharmacy, life expectancy, and patient preference should be weighed. Specific concerns with warfarin in the
geriatric population are discussed in the Venous Thromboembolism section and are pertinent to stroke. The lowest possible drug doses should be used in the elderly, including aspirin 81 mg.

Dose adjustment for geriatric patients with kidney and/or hepatic disease is always a consideration, as there is age-related decline in kidney and hepatic function. Extended-release dipyridamole with aspirin and aspirin monotherapy should be avoided in patients with estimated CrCl <10 mL/min, and clopidogrel therapy should be avoided in patients with severe kidney disease. Dipyridamole should also be used with caution in patients with severe hepatic impairment. Caution should also be exercised in older patients with syncope or orthostatic hypotension, as dipyridamole can exacerbate these conditions due to its vasodilatory properties.

**Venous Thromboembolism**

**Etiology, Epidemiology, and Clinical Presentation in the Geriatric Population**

The incidence of venous thromboembolism (VTE) is higher in the geriatric population compared with that in younger patients. Age should be considered when assessing a patient's risk of VTE. In a large study of 342,000 patients in France, the overall rate of VTE in the population was 1.83/1000 patients but 10/1000 in patients 75 or older. In addition to this higher risk, mortality associated with VTE is also higher in the geriatric population.

Risk factors for VTE, including malignancy, hormone replacement therapy, heart failure, severe lung disease, major surgery, and use of erythropoiesis-stimulating agents are more common in geriatrics. Immobility also plays a large role in determining risk. Paralysis from stroke can cause significant immobility, and recovery after surgery or procedures may put geriatric patients at higher risk. Older adults tend to have several of these risk factors, which are cumulative in conferring risk.

Orthopedic procedures such as total hip replacement, total knee replacement, and hip fracture surgeries are common in geriatrics. Immobility after these procedures carries a higher risk. Incidences of deep-vein thrombosis (DVT) from 7 to 14 days after these procedures in patients not undergoing VTE prophylaxis are as high as 40% to 60%. The administration of VTE prophylaxis reduces these incidences to 1% to 10% in the 3 months following surgery. Geriatric patients need aggressive monitoring and appropriate prophylaxis to prevent higher morbidity and mortality after these procedures and during their rehabilitation.

The clinical presentation of VTE in geriatrics is similar to that in younger people. Diseases such as heart failure and chronic obstructive pulmonary disease that occur more frequently in the older population can complicate the diagnosis of pulmonary embolism. Changes in the frequency or quality of shortness of breath and chest pain can be more difficult to detect in patients with those diseases, and symptoms related to those diseases can fluctuate. In addition, heart failure can cause significant lower extremity edema, which can complicate the diagnosis of DVT, although edema associated with DVT is typically unilateral. Advanced diabetic neuropathy and paralysis from stroke can also cause difficulty in recognizing changes in pain and temperature in lower extremities.

**Standard Adult Treatment Recommendations**

New guidelines for prevention and treatment of VTE were released in 2012 by ACCP. Risk assessment should be performed for each hospitalized patient and written policies and protocols should be in place to specify appropriate prophylaxis measures. Both mechanical and pharmacological methods are described in the guidelines. Treatment of acute VTE should be performed in an outpatient setting if possible, using low molecular weight heparin (LMWH) or fondaparinux initially. Duration of treatment depends on risk factors and identification of the cause of VTE. No distinctions are
made regarding the geriatric population in the guidelines, with the exception of recommending extra attention to dose adjustments of anticoagulants in those with kidney disease. Warfarin is the recommended long-term anticoagulant in the current guidelines. Rivaroxaban is an alternative to warfarin and has shown noninferiority to warfarin in treatment of VTE. Specific recommendations regarding VTE prevention in patients undergoing total hip and knee replacement or hip fracture surgeries are in the guidelines, as these procedures are commonly performed in geriatrics.105 Bleeding, kidney function, and development of postthrombotic syndromes should be monitored. Graduated compression stockings are recommended for prevention of postthrombotic syndrome for proximal DVT.

Treatment Recommendations in the Geriatric Population

The ACCP guidelines provide a strong basis for treatment recommendations; the majority of the analyses that form the basis for the guidelines include many patients over age 65, and some above 80 years.103-106 Treatment recommendations for prevention of VTE should be advocated for geriatrics. There is some evidence that physicians are less likely to use anticoagulation therapy in older people. The risk versus benefit ratio for VTE management is clearer than with indications such as atrial fibrillation, for which there may be more treatment alternatives. However, with respect to prophylaxis of VTE, physicians’ attitudes regarding risks associated with anticoagulation in elderly patients may be more of a factor. Mechanical methods should not be the sole method of prophylaxis, unless the patient is at high risk for bleeding. LMWH, fondaparinux, or warfarin should be used for VTE prophylaxis in patients undergoing total knee and total hip replacement. For patients undergoing hip fracture surgery, an additional option is low-dose unfractionated heparin.108 Considerations for dose adjustment of these agents for kidney disease are discussed below.

The duration of prophylaxis should be at least 10 days and up to 35 days after orthopedic surgery. Immobility and speed of recovery must be considered, and the duration of prophylaxis may need to be extended, depending on the course of recovery. Evidence for routine prophylaxis in nursing home patients and homebound geriatrics is not established, and no recommendations can be made.107

Evidence for treatment of VTE in geriatric patients is very similar to that in younger adults. The majority of the studies that form the basis for the ACCP guidelines include older adults. LMWH and fondaparinux administration facilitates outpatient treatment of DVT, which should be a goal for older patients as well. It is recommended that unfractionated heparin be used for initial treatment in patients with severe kidney disease, which could encompass some of the geriatric population. The duration of anticoagulation treatment of VTE depends, in part, on the number of VTE events experienced and whether risk factors can be eliminated. If immobility was a suspected cause of VTE, and is not expected to change, an older patient may continue anticoagulation treatment for longer than the recommended 3 months, even after a first event. Intensity of anticoagulation with warfarin for long-term treatment of VTE in the geriatric population should be an INR of 2.0–3.0.

The use of thrombolytic agents for management of pulmonary embolism should be reserved for patients with hemodynamic compromise.108 Contraindications for use of thrombolytics for pulmonary embolism include history of cerebrovascular accident, which may prohibit their use in geriatrics.108 Precaution should be used in patients older than 75 years, due to increased bleeding risk.108

Several issues pertaining to elderly patients must be considered regarding therapy with warfarin, which is used for long-term treatment of VTE and also for VTE prophylaxis. The initial recommended warfarin dose in elderly patients is ≤5 mg daily, according to the ACCP guidelines.109 In a large cohort study that included 2,359 patients ≥80 years of age, average weekly doses of warfarin were analyzed, strati-
fied by age. The investigators reported that the average weekly warfarin dose decreased by 0.4 mg for every year of age. The average daily dose for men and women 80 and older was 4.0 mg and 2.0–3.6 mg, respectively. The recommended initial daily dose of 5 mg would have been too high for 82% of women and 65% of men older than 70 in this study.

**KEY POINT:** In the geriatric population, therapy with warfarin should be initiated at 4–5 mg daily or less, with frequent early INR monitoring. If other factors such as heart failure, malnourishment (decline in total protein and albumin), or debilitation are present, an even lower dose should be considered.

The ACCP guidelines also suggest that for patients who desire less frequent INR monitoring, the intensity of anticoagulation can be lowered to a goal INR of 1.5–1.9 after the first 3 months of conventional therapy (INR 2.0–3.0). This lower target may work for geriatric patients, as they are perceived to be at higher risk for bleeding. However, the Extended Low-Intensity Anticoagulation for Thromboembolism Investigators (ELATE) trial compared the lower intensity warfarin regimen (INR 1.5–1.9) to the more conventional regimen (2.0–3.0) for prevention of VTE and found the conventional regimen to be more effective than lower-intensity warfarin, with incidences of recurrent VTE of 0.6% per patient-year and 1.9% per patient-year, respectively. The lower-intensity recurrence rate does provide benefit when compared with placebo rates in other studies. Furthermore, the lower-intensity regimen was not associated with a lower incidence of bleeding compared with the conventional regimen.

**Barriers to Treatment in the Geriatric Population**

Dose adjustments of LMWH and fondaparinux for patients with kidney disease must be considered. For patients requiring VTE prophylaxis with estimated CrCl <30 mL/min, the dose of enoxaparin should be 30 mg subcutaneously once daily. For patients requiring VTE treatment who have an estimated CrCl <30 mL/min, the enoxaparin dose should be 1 mg/kg once daily. The manufacturers of dalteparin and tinzaparin suggest caution with use of these drugs in patients with severe kidney disease and mention the potential need to monitor antifactor Xa activity. Fondaparinux should be used with caution in patients with estimated CrCl 30–50 mL/min, and the drug is contraindicated in patients with estimated CrCl <30 mL/min. These medications are administered subcutaneously, and the ability of the geriatric patient to perform self-injections, or the ability of a caregiver to consistently administer injections, should be evaluated before the patient is placed on outpatient treatment.

The same concerns with rivaroxaban discussed in the Atrial Fibrillation section apply to VTE. Geriatric patients may have less access to transportation and may have difficulty meeting the monitoring requirements for warfarin therapy. Alternatives in this case may include continued treatment with LMWH/fondaparinux or the possible use of point-of-care INR monitoring. Medicare now has expanded coverage for point-of-care testing for patients undergoing chronic warfarin therapy for VTE. It is only approved after the patient has been on anticoagulation therapy for 3 months, has undergone face-to-face education, and is not monitoring more than once weekly. The patient's dexterity should also be assessed to determine whether he or she has the capacity to perform this monitoring.

Older adults may be more sensitive to the effects of warfarin. As discussed previously, elderly patients generally require lower warfarin doses, and higher initiation doses in the past may have contributed to some of the data indicating a higher risk of bleeding. Lower body weight and volume of distribution may also be factors.

Hypoalbuminemia, malnourishment, or decreased dietary vitamin K intake may also contribute to higher sensitivity. A few studies have suggested that receptor sensitivity may be
altered or greater inhibition of vitamin K–dependent clotting factors may occur in the elderly, but currently there are few data to support this. Management of warfarin therapy is also complicated by the potential for numerous drug interactions, as polypharmacy tends to be more common in geriatrics.

Bleeding is a major concern for any patient on anticoagulation therapy, and even more so for the elderly. The risk of falls must be assessed and considered in the risk versus benefit analysis, as discussed in the Atrial Fibrillation section.
Case 1: Deep-Vein Thrombosis

Setting:
Ambulatory anticoagulation clinic.

Subjective:
JT is an 80-year-old male referred to your anticoagulation clinic for initiation of therapy with enoxaparin and warfarin after his deep-vein thrombosis diagnosis today. The patient presents using walker and appears very unsteady in movement.

Past Medical History:
Hypertension, osteoarthritis, heart failure (left ventricular ejection fraction 30%), hyperlipidemia, CKD, coronary artery disease, coronary artery bypass graft ×3 in 2001.

Medications:
Hydrochlorothiazide 25 mg daily, lisinopril 10 mg daily, metoprolol XL 100 mg daily, furosemide 20 mg daily as needed, aspirin 81 mg daily, simvastatin 40 mg bedtime, ibuprofen 600 mg three times daily prn.

Allergies:
NKDA.

Social History:
Married to wife ×60 years. She sets up a medication organizer weekly for JT and reports that he is adherent to regimen. Nonsmoker. Drinks 1 beer nightly and 1 cup of regular coffee each morning.

Family History:
Mother: diabetes and Alzheimer disease
Brother: Parkinson disease

Objective:
Wt 168 lb, Ht 70”, BP 125/72 mmHg, AST 27 international units/L (15–46), ALT 48 international units/L (11–66), creatinine 2.2 mg/dL.

Assessment:
1. Deep-vein thrombosis requiring anticoagulation with warfarin and enoxaparin complicated by kidney disease, heart failure, and potential falls risk.
2. Heart failure well controlled on diuretic, beta blocker, and ACE inhibitor. Ibuprofen should not be used in this patient, because it is an NSAID.
3. Hypertension well controlled. Hydrochlorothiazide not beneficial in patients with CrCl <30 mL/min.

Plan:
1. Given JT’s significantly impaired renal function (estimated CrCl 28 mL/min), enoxaparin should be administered at a dose of 1 mg/kg once daily, based on the patient’s weight of 76 kilograms (~ 80 mg once daily). Assess ability to perform injections or educate caregiver on technique for injections. Assess the risk of falls with questions regarding frequency of falls, daily activities, orthostatic symptoms, etc. Warfarin therapy should be initiated at a dose <5 mg daily in this patient given his age, concomitant medications, mobility problems, and heart failure. Recommend warfarin 3 mg daily. Re-check INR in 5–7 days. JT likely requires more frequent monitoring as he is at high risk for complications for the above reasons.
2. Continue current heart failure therapy. Discontinue ibuprofen and recommend scheduled acetaminophen for osteoarthritis pain.

3. Discontinue hydrochlorothiazide. Recommend home blood pressure monitoring and, if needed, increase lisinopril dose.

Rationale:
1. Enoxaparin dose must be reduced due to diminished kidney function. Warfarin therapy is initiated at lower dose because of age, medications, falls risk, and heart failure. Osteoarthritis can interfere with ability to perform injections. Potential for falls needs special attention, as falls may lead to more severe complications for patients on warfarin.

2. Diuretics, ACE inhibitors, and beta blockers are all therapies indicated for heart failure and should be used in the geriatric population. Ibuprofen is an NSAID that can exacerbate fluid retention in heart failure, complicate kidney disease, and lead to higher risk of GI bleeds in patients taking warfarin.

3. Hydrochlorothiazide provides little blood pressure benefit for patients with CrCl <30 mL/min. Home blood pressures can be used to assess control off medication. Lisinopril is not at target dose for heart failure, and the dose could be increased to benefit both heart failure and hypertension.

Case Summary:
The geriatric patient needs a thorough assessment when anticoagulation therapy is initiated. Elderly patients are typically taking a larger number of medications and have more disease states and social issues that need to be addressed compared with younger patients.
Case 2: Orthostatic Hypotension

Setting:
Long-term care facility.

Subjective:
LM is an 89-year-old female resident of a long-term care facility who has been experiencing multiple falls, some resulting in injuries such as bruising and skin tears. Over the last 6 months, her ambulation status has declined from independent to wheelchair level. She complains of pain in her legs when walking more than short distances across the nursing unit.

Past Medical History:
Hypertension, Alzheimer disease, hypothyroidism, osteoarthritis.

Medications:
Amlodipine 10 mg daily, donepezil 10 mg at bedtime, levothyroxine 0.88 mg every morning, celecoxib 200 mg daily, furosemide 40 mg every morning.

Allergies:
NKDA.

Social History:
LM is widowed, with two adult children living in town; retired photographer; and owner of an art supply store.

Family History:
Unknown

Objective:
Wt 129 lb, Ht 64”, BP (supine) 177/82 mmHg, BP (standing) 105/60 mmHg, P 78/min.

Physical Examination:
HEENT: Normocephalic, no evidence of trauma, PERRLA, EOMI, dry mucous membranes
CV: Regular rate and rhythm
Respiratory: Clear to auscultation bilaterally
Abdomen: Soft, nontender, no masses or guarding
G/U: Skin intact, assisted with toileting and personal hygiene by staff
Extremities: Bilateral 2+ edema to lower extremities; skin dry, dark bruising and skin tear to right elbow and forearm
Neuro: Alert and oriented to person only. MMSE 18/30, stable over last 12 months

Labs:
TSH 2.45, Free T4 0.98
Serum chemistry: Na 135, K 3.8, Cl 99, CO₂ 25, glucose 101, SCr 0.9, BUN 42
CBC: WBC 7.0, RBC 4.5, Hgb 11.9, Hct 34.1, platelet 255
UA: clear

Assessment:
1. Using the faces pain scale, no pain is occurring at rest. On walking LM complains of moderate-severe pain.
2. Orthostatic hypotension resulting in falls, possibly associated with medications. While each of LM’s medications could relate to falls by some mechanism, the drug of primary concern is furosemide.
3. Medication without clear indication: furosemide. This is being used to treat edema, but the etiology of the edema is not clear and could be induced or exacerbated by her current drug therapy.

4. Decrease in ambulation status associated with increased pain on walking and recent falls.

**Plan:**
Recommend discontinuation of amlodipine, celecoxib, and furosemide, and replacement with hydrochlorothiazide 25 mg daily and acetaminophen 500 mg four times daily. Recommend physician evaluation for peripheral vascular disease and IC and to rule out heart failure or other causes of edema. Monitor vitals (including orthostatic hypotension assessments), edema, and pain daily, and follow-up serum chemistry within 30 days.

**Rationale:**
1. LM may be experiencing falls due to orthostatic hypotension associated with uncontrolled supine hypertension and an unnecessary loop diuretic. Her sodium and potassium, though in the normal range, are lower than optimal and continued use of a diuretic without potassium supplementation can further exacerbate electrolyte status.

2. Her SCr:BUN ratio and dry mucous membranes suggest she is a little dehydrated. Although she is currently experiencing bilateral edema, she does not have a diagnosis that explains the cause of the edema. She currently takes two medications that could be causing, or at least exacerbating, the edema: amlodipine and celecoxib. If edema were to improve or resolve on discontinuation, the furosemide would not be necessary. The amlodipine is not currently controlling her hypertension. Hydrochlorothiazide alone may not either, but it is a reasonable initial choice and combination therapy can be considered if necessary.

3. It is difficult to assess the efficacy of celecoxib for osteoarthritis. There is no pain at rest, and she may achieve similar pain control with scheduled acetaminophen while avoiding NSAID side effects. The pain on walking could suggest peripheral vascular disease with IC, and she should be evaluated for this. Ruling out heart failure as a cause of her edema is important because the choice of drug therapy for PVD depends on her comorbidities. LM does have other risk factors for dizziness and falls, including dementia, cholinesterase inhibitor use, and a thyroid disorder. However, these conditions have been stable on the current drug therapy, and any considerations for adjustments should be deferred until after the effects of the above changes are observed.

**Case Summary:**
LM’s case illustrates several examples of drug therapy problems in a frail elderly patient. These include (1) the use of medication to treat a symptom without investigating the underlying cause, (2) a prescribing cascade where new medications are prescribed to treat side effects of existing medications, (3) failure to assess efficacy of the drug regimen, and (4) a potential unrecognized and untreated medical condition.

Furosemide has been prescribed to treat edema, but it is not clear if the edema was caused by medication side effects, PVD, or heart failure. Failure to assess the root cause has resulted in the lack of intervention for a potential underlying problem. Also, the new medication prescribed to treat the edema is now causing new problems, such as orthostatic hypotension and dehydration, and LM continues to experience supine hypertension and pain interfering with ambulation despite amlodipine and celecoxib use. The underlying problem is cardiovascular but has implications for functional status and quality of life.
Chapter Summary

The prevalence and incidence of vascular diseases increases with advancing age, and are highest in the elderly population. Treatment guidelines exist for many cardiovascular diseases, but in many instances specific recommendations for elderly patients are lacking. For some treatments, elderly patients derive greater benefit than younger patients. However, in many cases, elderly patients are more susceptible to the adverse effects associated with drugs used to treat cardiovascular diseases, and close monitoring in this population is particularly warranted.

Self-Assessment Questions

1. How does the presence or absence of hypertension in elderly patients in different subgroups affect their expected survival, and how do blood pressure goals differ in the subgroups?

2. What are some potential barriers in diagnosing peripheral arterial disease and the risks associated with not overcoming them?

3. What criteria are used to determine whether an elderly patient with atrial fibrillation should receive warfarin or aspirin for stroke prevention?

4. What are the documented benefits of treating elevated serum LDL cholesterol in elderly patients?

5. What are the risks and benefits of using beta blocker, ACE inhibitors, and digoxin in elderly patients with heart failure?

6. How does the risk of stroke change with every decade over age 55?

7. What are some comorbidities in elderly patients who have complicated anticoagulation for VTE?

References


Clinical Pearls

- Elderly patients can have atypical presentations of heart failure, with symptoms such as anorexia, confusion, generalized weakness, and fatigue. Echocardiography should be used to identify heart failure and determine left ventricular function to guide therapy.

- An auscultatory gap is a common phenomenon among older patients with hypertension. This is a phenomenon of particular importance to the elderly patient. If palpation of the radial pulse is not performed to ensure adequate inflation of the cuff in an elderly patient, the re-emergence of Korotkoff sounds at the bottom of the gap can be mistaken as the systolic pressure. This can result in a falsely low reading.


Learning Objectives

1. Critically review the medical literature representing treatment of chronic obstructive pulmonary disease (COPD), asthma, and tuberculosis (TB) in older adults.

2. Assess the applicability of general adult treatment guidelines for COPD, asthma, and TB to older adults.

3. Recommend appropriate drug therapy and treatment goals for various respiratory disorders in older adults.

4. Describe common problems encountered by older adults associated with therapies for respiratory disorders and recommend solutions to these problems.

Key Terms and Definitions

IMMUNOSENESCENCE: The waning of the immune system that occurs with age.

NEBULIZER: A device used to disperse liquid medicine in a mist of extremely fine particles; useful in delivering medicine to the lower respiratory tract.

REACTIVATION: A TB stage that occurs from a previously dormant focus seeded at the time of primary infection. Symptoms of cough, weight loss, and fatigue develop insidiously over weeks to months before diagnosis.

SPIROMETRY: Study of air volume and flow rate within the lungs. Normal values are based on age, gender, and height and are expressed as a percentage of a person’s predicted value. Key measurements include forced vital capacity (FVC) and forced expiratory volume over the first second (FEV-1).
A host of age-related changes occur in the respiratory system. Although some of these changes are normal in aging, most are secondary to environmental effects or complications due to specific disease states. When pulmonary insults occur in the elderly patient, such as COPD, asthma, and infection, the loss of reserve capacity in the lung prevents adequate response to the stressors imposed. Pulmonary decompensation can be rapid and difficult to reverse. This is readily apparent in the frailest of patients.

This chapter covers respiratory-related illnesses common in the older population, including COPD, asthma, and TB. Pneumonia and influenza are discussed in Chapter 17. Institutionalized patients have important differences from those in the community regarding treatment of these diseases. However, in any setting, adequate use of preventive measures and rapid response when exacerbations occur can reduce the morbidity and mortality associated with these illnesses. Pharmacists must take a leading role in ensuring patients, caregivers, and other healthcare professionals are educated to recognize and implement optimal pharmacotherapy to prevent and/or treat respiratory illnesses in the older patient.

Chronic Obstructive Pulmonary Disease and Asthma

Etiology, Epidemiology, and Clinical Presentation Specific to Geriatrics

Respiratory diseases are common disorders in older adults and account for significant morbidity and mortality. COPD is the third leading cause of death in the United States and affects 20% of adults. The prevalence of asthma in older adults is difficult to assess due to underdiagnosis, misdiagnosis, and undertreatment; however, most studies indicate a prevalence of approximately 7%. Differentiating the two conditions can be problematic for the experienced clinician, especially because asthma and COPD may coexist in the same patient.

With respiratory disorders being so common, special attention should focus on the issues that are unique in the elderly: potential for medication adverse effects, especially in those patients with multiple medical comorbidities; drug interactions in patients receiving polypharmacy, particularly medications that may worsen asthma and COPD; and issues of effective medication delivery, specifically with reference to inhaled medications. In addition, many age-related changes occur within the respiratory system that can affect the course of both asthma and COPD.

Age-related changes affecting the respiratory system include

- loss of height secondary to osteoporosis, leading to a decrease in lung volume,
- neurologic conditions affecting the swallowing mechanism, leading to aspiration,
- decreased perception of bronchoconstriction despite similar levels of decreases in forced expiratory volume over 1 second (FEV-1) after a methacholine challenge test, and
- decreased bronchodilator response to inhaled beta agonists (no data to support any age-related difference in response to inhaled anticholinergic medications).

The misconception that asthma is a childhood disease causes symptoms to be overlooked by both patients and physicians. A majority of elderly patients who develop asthma after the age of 65 have their first asthmatic symptoms preceded immediately or concomitantly with an upper respiratory tract infection. This may delay the diagnosis of asthma, because patients attribute their respiratory symptoms to lingering effects from the upper respiratory tract infection. Other conditions and diseases may present with respiratory symptoms, such as heart failure.
and gastroesophageal reflux, in which cough is a common complaint as it is with asthma. Treatment of asthma is more complicated in older patients compared to younger patients. Although younger patients may be managed with medications as needed, older patients most often require continuous therapy complicated by frequent dosing with multiple medications.

**Summary of Standard Treatment in the General Adult Population**

The management of COPD has been summarized in national and international guidelines that stress similar treatment modalities. The Global Initiative for Chronic Obstructive Lung Disease was designed to increase awareness of COPD and improve prevention and management with the ultimate goal of reducing disease-related morbidity and mortality. The goals of treatment for COPD are to improve quality of life, exercise tolerance, sleep quality, and survival and to reduce dyspnea, nocturnal symptoms, exacerbations, use of rescue medications, and hospitalizations. The diagnosis of COPD should be considered in any patient who has dyspnea, chronic cough, or sputum production, and/or a history of exposure to risk factors for the disease. The diagnosis should be confirmed by spirometry. A post-bronchodilator FEV$_1$/FVC ratio <0.70 confirms the presence of airflow limitation that is not fully reversible. The FEV$_1$/FVC ratio is used to stratify the severity of airflow limitation. Symptoms can be quantified using the Modified British Medical Research Council questionnaire on breathlessness or the COPD Assessment Test. Assessment of a patient's risk of COPD exacerbation is based on his or her exacerbation history. Treatment regimens include medications with different mechanisms of action (Table 8-1). Depending on the severity of COPD, the guidelines recommend first and alternative treatment choices (Table 8-2). However, only smoking cessation and supplemental oxygen therapies have been proven to improve the course of COPD. Smoking cessation is most effective in early disease, but all patients who smoke should be encouraged to quit.

Similar to COPD, a stepwise approach to the treatment of asthma is recommended. Step 1 utilizes short-acting beta agonists on an as-needed basis; steps 2–4 emphasize inhaled corticosteroids (ICS) as the preferred regimen, with the daily dose of ICS increasing as the steps progress. Alternative treatment options include leukotriene receptor modifiers, cromolyn, and theophylline. Omalizumab should be considered in patients who have allergies, although there are limited data on its efficacy in older adults. These treatment steps have been designed for the general adult population and may be applied to older adults with some modifications.

For both COPD and asthma, proper inhaler technique is critical to successful therapy. The following strategies should be employed when counseling patients using inhalers:

- Be familiar with various inhaler devices and how to use them; placebo devices are a valuable training aid
- Demonstrate the technique to the patient
- Encourage patients to demonstrate the use of their inhaler
- Re-check inhaler technique at each visit until the patient has mastered the technique; consider re-checking this every 2–3 months thereafter
- Reinforce that spacer devices are an essential tool
- Minimize the number and types of inhaler devices
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<th>Class: Medication Examples</th>
<th>Indications for Use</th>
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| Short-acting β agonists (SABA):  
Inhaled and oral bronchodilators  
Albuterol  
Pirbuterol terbutaline sulfate (oral tablets only)  
Levalbuterol hydrochloride  
Levalbuterol tartrate | Asthma: Treatment of choice for relief of acute symptoms and prevention of exercise-induced bronchospasm; generally used as needed.  
COPD: For relief of acute symptoms. | Asthma: Use of SABA >2 days a week for symptom relief (not prevention of EIB) generally indicates inadequate asthma control and need for initiating or intensifying anti-inflammatory therapy.  
COPD: Improves breathlessness but not other patient-oriented outcomes. In stable COPD there is an associated improvement in FEV-1. | Combinations of bronchodilators improve efficacy and reduce risk of AEs versus increasing the dose of a single agent.  
This sound strategy supports combination therapy using ipratropium and albuterol, for example, rather than quadrupling the dose of either one of those agents alone.  
Possible SE: tachycardia, palpitations, tremor, feeling nervous, insomnia, HA, N/V. Geriatric patients may be more susceptible to these effects. |
| Anticholinergics: Inhaled bronchodilators  
Ipratropium bromide  
Tiotropium | Asthma: Ipratropium may be used as an alternative bronchodilator for patients intolerant of SABA.  
COPD: May be more effective than long-acting β agonist (LABA) in relieving the symptoms of COPD. | Asthma: Effective as bronchodilator but not as potent as β agonists.  
Ipratropium provides additive benefit to SABA in moderate or severe exacerbations not responding to β agonists alone.  
COPD: Improves symptoms and quality of life and decreases exacerbations, hospitalizations, and deaths; improves sleep. Decreases rescue inhaler use and office visits. | Inhaled ipratropium has an excellent safety profile in the elderly, and it should be considered for use when additional bronchodilator therapy is necessary. Ipratropium has a slow onset of action; it requires 30–60 min for maximal effect.  
Possible AE: Dry mouth, abnormal taste in mouth, bitter, nasal congestion, dry nasal mucosa, tachycardia.  
Tiotropium: Ensure that patient has the dexterity to place the capsule in the HandiHaler; do not swallow the capsule—for inhalation use only. |
Table 8-1. Commonly Used Drugs in the Management of COPD and Asthma (cont’d)

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Asthma: The most effective long-term control therapy for persistent asthma regardless of severity.

Patient should be started on higher and more frequent doses and then tapered down once control has been achieved. Response is delayed with symptom improvement occurring within the first 1–2 wk in most patients and full therapeutic benefits in 4–8 wk.

Risk of systemic toxicity minimal with low to moderate doses and increases with high doses (>1000 mcg/day). Local AEs (e.g., oropharyngeal candidiasis, hoarseness, cough, and dysphonia) can be reduced by use of a spacer device and rinsing mouth after use.

Use the lowest dose that maintains asthma control. Assess patient’s inhaler technique, adherence, and environmental measures before increasing dose. Adding a LABA to a low or medium dose of inhaled corticosteroids may be more effective than doubling the dose of steroids to maintain asthma control.

COPD: Decreases exacerbations in patients with moderate to severe disease. No effect on mortality.

Long-term use of inhaled corticosteroids at recommended doses has been associated with a good safety profile. AEs are dose related. Local effects of the mouth and pharynx include candidiasis and dysphonia. Systemic absorption of inhaled corticosteroids has been associated with skin bruising, cataracts, and reduced bone mineral density. An increase risk of pneumonia has been associated with high doses (1000 mcg/day) of fluticasone.
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<tr>
<td>Inhaled bronchodilator</td>
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<tr>
<td>Formoterol</td>
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<tr>
<td>Salmeterol</td>
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<tr>
<td><strong>Asthma:</strong> Used as adjunctive long-term therapy with inhaled corticosteroids, which is more effective than increasing the dose of corticosteroids alone. Can be used for nocturnal asthma.</td>
<td><strong>NOT used as monotherapy due to absence of anti-inflammatory properties. NOT effective for acute severe asthma due to slow onset (20–30 min). Formoterol has faster onset than salmeterol. Need to continue short-acting β agonist for acute exacerbations while on LABAs.</strong></td>
<td><strong>Use in the elderly should be closely monitored. Geriatric patients may be more susceptible to SEs of β agonists (e.g., tachycardia, palpitations, tremor). This risk is higher in patients with pre-existing coronary artery disease. Other SEs include nervousness, insomnia, HA, and N/V. May cause dose-dependent drop in serum potassium and QT interval prolongation; use cautiously in patients with arrhythmia and pre-existing coronary artery disease. Although not clearly established, airway responsiveness to β-agonist medications may also decrease with age.</strong></td>
<td></td>
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<tr>
<td>Methylxanthine: Oral bronchodilators</td>
<td>Asthma: Sustained-release theophylline may be used as alternative, not preferred, therapy for step 2 (mild persistent asthma). It may be also used as an adjunctive with inhaled corticosteroids.</td>
<td>Rarely used in practice. Monitoring of theophylline concentration is essential. Severe cardiac arrhythmia, seizures, and death can occur at serum concentration only twofold greater than optimal therapeutic concentration.</td>
<td><strong>Use not recommended due to safety concern. Patients over age 75 have a 16-fold greater risk of life-threatening events or death than patients under age 25 at comparable serum theophylline level. Dose should be reduced. Elderly patients should be started with a 25% reduction of the adult dose.</strong></td>
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<tr>
<td>Theophylline</td>
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<tr>
<td>Combined medication: Inhaled bronchodilator and steroid</td>
<td>Asthma: Use is recommended for step 3 (moderate persistent asthma). COPD: Use is recommended in Group D patients with many symptoms and high risk for exacerbations.</td>
<td>The combination gives the advantage of providing bronchodilation while reducing airway inflammation. LABA also allows reduction in corticosteroid dosage (by 50%). Onset is rapid (within 1 wk). Compliance can be also improved with the combination.</td>
<td><strong>Refer to each component.</strong></td>
</tr>
<tr>
<td>Budesonide and formoterol</td>
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<tr>
<td>Fluticasone and salmeterol</td>
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<tr>
<td>Fluticasone and vilaanterol</td>
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</tbody>
</table>
### Table 8-1. Commonly Used Drugs in the Management of COPD and Asthma (cont’d)

<table>
<thead>
<tr>
<th><strong>Class:</strong> Medication Examples</th>
<th><strong>Indications for Use</strong></th>
<th><strong>General Adult Treatment Principles</strong></th>
<th><strong>Geriatric Considerations</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>Corticosteroids: Oral anti-inflammatory</td>
<td>Asthma: Indicated in patients with acute severe asthma not responding completely to aggressive inhaled β agonists. Also used long term to treat patients with severe persistent asthma. COPD: Long-term treatment with oral corticosteroids is not recommended in COPD. Can be used for short periods for management of COPD exacerbations.</td>
<td>May take 6–8 hr for pulmonary function improvement. Most patients achieve 70% predicted FEV-1 within 48 hr and 80% by day 6. Full dose should be continued until patient’s peak flow reaches 80% of predicted normal or personal best. Tapering the steroid dosage after short course is unnecessary. The following attempts should be made: (1) optimize therapy with inhaled corticosteroids, (2) keep oral steroids to the minimum dose possible, (3) use relatively short-acting agents (e.g., prednisone and methylprednisolone), (4) attempt to control symptoms with alternate-day dosing.</td>
<td>Long-term use of corticosteroids may lead to or exacerbate osteoarthritis, diabetes, hypertension, cataracts, and (rarely) depression of the immune system and susceptibility to infections. This can be troublesome because many of these complications occur in the elderly even without steroid use. Myopathy, increased skin fragility, loss of attention span and memory, and mood swings may also occur in geriatric patients with long-term steroid use. Monitor closely with long-term steroid use.</td>
</tr>
<tr>
<td>Methylprednisolone</td>
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<tr>
<td>Prednisone</td>
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<tr>
<td>Dexamethasone</td>
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<tr>
<td>Leukotriene modifiers: Oral anti-inflammatory</td>
<td>Asthma: Effective in prevention of allergen-induced, exercise-induced, and aspirin-induced asthma.</td>
<td>Can also be used as adjunctive therapy with inhaled corticosteroids. Can be used as daily medication for mild persistent asthma but is less preferred than low-dose inhaled corticosteroids. Liver function monitoring is essential. Possible AEs: headache, nausea, diarrhea, infection.</td>
<td>Geriatric patients may be more susceptible to some of the AEs (e.g., headache, mild infection). Females &gt;65 years of age appear to be at an increased risk for ALT elevations. QT interval prolongation is possible with zileuton. Montelukast appears to be the safest of the three.</td>
</tr>
<tr>
<td>Montelukast</td>
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<tr>
<td>Zafirlukast</td>
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<tr>
<td>Zileuton</td>
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<tr>
<td>Mast cell stabilizers: Inhaled anti-inflammatory</td>
<td>Asthma: Indicated for prophylaxis of mild persistent asthma (step 2).</td>
<td>May be particularly effective for allergic asthmatics on a seasonal basis. May also be used as preventive therapy before exercise or unavoidable exposure to known allergens. Coughing and wheezing are possible after inhalation of each agent; bad taste and headache are possible after nedocromil use.</td>
<td>Well tolerated.</td>
</tr>
<tr>
<td>Cromolyn sodium</td>
<td></td>
<td></td>
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<tr>
<td>Nedocromil sodium</td>
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</tr>
<tr>
<td>Class: Medication Examples</td>
<td>Indications for Use</td>
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<td>Geriatric Considerations</td>
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<tr>
<td>Monoclonal antibody:</td>
<td>Asthma: Indicated</td>
<td>Dose is based on IgE serum levels prior to treatment and body weight. Dosing adjustment during treatment should be based on significant changes in body weight, NOT IgE levels during or &lt;1 year following discontinuation of therapy. Possible SE: injection-site reactions, anaphylaxis, viral infection, upper respiratory tract infection, sinusitis, headache, sore throat.</td>
<td>Specific geriatric considerations have not been established. Elderly patients might be more susceptible to AEs.</td>
</tr>
<tr>
<td>Anti-allergen</td>
<td>for treatment of moderate to severe persistent allergic asthma not well controlled by high doses of inhaled corticosteroids.</td>
<td></td>
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<tr>
<td>Omalizumab</td>
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</tbody>
</table>

AE, adverse effect; ALT, alanine aminotransferase; EIB, exercise-induced bronchospasm; HA, headache; IgE, immunoglobulin E; N/V, nausea and vomiting.
<table>
<thead>
<tr>
<th>Patient Group</th>
<th>Recommended First Choice</th>
<th>Alternative Choice</th>
<th>Other Possible Treatments</th>
</tr>
</thead>
<tbody>
<tr>
<td>A (few symptoms, low risk of exacerbation)</td>
<td>Short-acting anticholinergic prn or short-acting $\beta_2$ agonist prn</td>
<td>Long-acting anticholinergic or long-acting $\beta_2$ agonist or short-acting $\beta_2$ agonist and short-acting anticholinergic</td>
<td>Theophylline</td>
</tr>
<tr>
<td>B (more significant symptoms but low risk of exacerbation)</td>
<td>Long-acting anticholinergic or long-acting $\beta_2$ agonist</td>
<td>Long-acting anticholinergic and long-acting $\beta_2$ agonist</td>
<td>Short-acting $\beta_2$ agonist and/or short-acting anticholinergic</td>
</tr>
<tr>
<td>C (few symptoms but high risk for exacerbations)</td>
<td>Inhaled corticosteroid + long-acting $\beta_2$ agonist or long-acting anticholinergic</td>
<td>Long-acting anticholinergic and long-acting $\beta_2$ agonist or long-acting anticholinergic and phosphodiesterase-4 inhibitor or long-acting $\beta_2$ agonist and phosphodiesterase-4 inhibitor</td>
<td>Short-acting $\beta_2$ agonist and/or short-acting anticholinergic</td>
</tr>
<tr>
<td>D (many symptoms and high risk for exacerbations)</td>
<td>Inhaled corticosteroid + long-acting $\beta_2$ agonist and/or long-acting anticholinergic</td>
<td>Inhaled corticosteroid + long-acting $\beta_2$ agonist and long-acting anticholinergic or inhaled corticosteroid + long-acting $\beta_2$ agonist and phosphodiesterase-4 inhibitor or long-acting anticholinergic and long-acting $\beta_2$ agonist or long-acting anticholinergic and phosphodiesterase-4 inhibitor</td>
<td>Short-acting $\beta_2$ agonist and/or short-acting anticholinergic</td>
</tr>
</tbody>
</table>

prn, as needed.

**Review of Evidence Base
Supporting Treatment Recommendations for Elderly Patients**

A systematic search of the medical literature evaluated the inclusion of older adults in clinical trials in COPD. After reviewing two decades’ worth of information, the authors concluded that although older adults were not specifically excluded from the trials, they were under-represented. The average age of the subjects recruited was 58–69 years, and very few subjects over the age of 80 years participated in the trials. In addition, subjects with comorbidities such as asthma, other respiratory disorders, and cardiovascular diseases were excluded from these trials. Approximately 40% of clinical trials excluded subjects with electrocardiogram abnormalities and cardiovascular disease, such as recent myocardial infarction, unstable angina, arrhythmias, and heart failure. This is disconcerting, given the potential for cardiovascular side effects associated with therapy for COPD (e.g., QT interval prolongation, tachycardia and other arrhythmias, worsening of myocardial ischemia and congestive heart failure, electrolyte disturbances).

Another systematic search of the medical literature evaluated the inclusion of older adults in clinical trials in asthma. The average age of the subjects in these clinical trials ranged from 25 to 49 years, with some trials excluding older adults. Of the articles reviewed, approximately 17% had no specific exclusions or contained information on exclusions. Existing clinical trials need to be interpreted with caution, because exclusion of patients of advanced age and multiple medical comorbidities was common. The asthma treatment algorithms emphasize long-term pharmacologic treatment, with careful attention placed on self-management.

Inhaled beta agonists can cause both pulmonary and extrapulmonary adverse effects. In a meta-analysis of randomized placebo-controlled trials of beta agonists in 6,623 patients (mean age 52.2 years) with obstructive airway disease, cardiac adverse events were classified as mild, including minor changes in heart rate and clinically unimportant changes in the level of serum potassium. There was an increase in the risk for adverse cardiovascular events (relative risk 2.5), largely caused by an increase in the risk of sinus tachycardia. The likelihood of major cardiovascular events did not reach statistical significance. In absolute terms, approximately one additional event occurred in the beta-agonist group for every 200 patients treated over a 6-month period. The Salmeterol and Fluticasone Propionate and Survival in Chronic Obstructive Pulmonary Disease trial, commonly referred to as the TORCH trial (n = 6184, 1,542 patients in the salmeterol arm, mean age 65 years) found that cardiovascular causes contributed to mortality in 3% of patients, with no significant difference between the salmeterol and placebo groups. The Salmeterol Multi-Center Research Trial (SMART), designed to test the safety of salmeterol, had about 26,000 participants but was stopped early because of safety concerns. As a result of the study, the Food and Drug Administration (FDA) issued a public health advisory for long-acting beta-2 agonists (LABA). It warned that these medications can cause a “small but significant risk in asthma-related deaths.” The FDA also required the addition of a boxed warning to LABAs.

There has been considerable debate over the use of beta agonists in the management of moderate and severe COPD. Supporters of beta agonists believe that clinical trials clearly show short-acting beta-2 agonists and LABAs improve dyspnea, quality of life, and reduce respiratory exacerbations in patients with COPD. Also, proponents argue that anticholinergics have equal or superior efficacy to beta agonists in improving lung function parameters without creating tolerance over time as seen with regular use of beta agonists. In elderly asthmatic patients, LABA should be used only in combination with ICS due to these safety concerns and the potential for cardiac comorbidities. It would be prudent to carefully assess the cardiac risk factors before instituting a LABA in a patient with COPD.
In patients with moderate to severe COPD, ICS should be used to reduce exacerbations. A meta-analysis of 12 randomized controlled trials assessing ICS demonstrated one fewer exacerbation for every 12 patients with moderate-to-severe disease who were treated for 18 months. However, ICS are associated with a variety of adverse effects; the most common are the local effects in the upper airways, such as thrush and dysphonia. These complications can be minimized through the use of spacers and rinsing the mouth after inhalation of the drug. Due to the increased risk of osteoporosis and osteopenia in older adults, treatment with ICS has been evaluated to examine if these agents pose any increased risk of reduced bone mineral density. In the TORCH trial, patients treated with fluticasone alone or in combination with salmeterol reported a nonsignificant increase in the incidence of fractures compared with placebo (5.4%, 6.3%, and 5.1% respectively). In a subset of TORCH, in which participants (n = 658) were specifically assessed for changes in bone mineral density, the prevalence of osteopenia was significant. Specifically, about 70% of all patients had osteopenia or osteoporosis, indicating that abnormal bone health is a common problem in COPD. Higher doses of ICS, such as those used in the management of asthma, have been associated with increased bone turnover, but data on bone mineral density and fracture at these doses are not available. Those patients requiring oral corticosteroids for management of their respiratory disease should be on adequate doses of calcium and vitamin D, at a minimum. Bisphosphonates are the drugs of choice for the treatment and prevention of glucocorticoid-induced osteoporosis and should be considered if the patient will require continuous glucocorticoid therapy, unless there is a documented contraindication.

Cataracts and glaucoma have also been associated with ICS. The TORCH study performed slit-lamp examinations in a safety subset of 658 subjects using high-dose ICS (fluticasone 500 mcg, twice daily). Only 29% of patients did not have cataracts at baseline examination. There were no differences in the development of new cataracts compared with the placebo group. Thus, the relationship of ICS to cataract formation is not totally clear. In a systematic review of the literature, an expert panel found grade C evidence that ICS are associated with cataracts in young asthma patients; however, the risk may be elevated in older patients. This same expert panel found the risk of glaucoma with ICS use to be small, probably dose dependent, and found insufficient evidence to conclude whether any specific ICS formulation had an increased risk.

Common Problems Encountered When Treating Elderly Patients with Chronic Obstructive Pulmonary Disease

Elderly patients may use inhaler devices improperly due to poor eyesight, poor hand strength, arthritis, and coordination difficulties. Older adults are underrepresented in studies evaluating different inhaler types, and results are often extrapolated from predominately younger adults with asthma, not COPD. However, most patients, regardless of their age, should be able to acquire and maintain adequate technique when given appropriate instruction, with the exception of those patients with significant cognitive impairment. Spacer devices may be used with metered-dose inhalers (MDIs) when patients have difficulty with hand-breath coordination. Spacers improve drug delivery and reduce systemic absorption. Common problems encountered by older adults include difficulty connecting the MDI to the spacer, difficulty activating the device, and unnecessary repetitive firing into the spacer. Up to 85% of patients who were prescribed spacer devices did not use them.

Dry-powder inhalers (DPIs) have been developed to overcome difficulties encountered with MDIs and have been viewed as more patient friendly by patients and healthcare providers. In general, DPIs require a higher peak inspiratory flow (PIF) than MDIs for effective drug delivery, because a minimum inspiratory flow is required to disaggregate and disperse the drug powder.
in the inhaled airstream. In a study specifically designed to assess the use of DPIs in elderly patients with mild and moderate COPD, a large percentage of participants were unable to generate adequate PIFs for optimum use of some popular DPI devices. An analysis showed that both age and COPD disease severity were independent variables influencing PIF.

**KEY POINT:** Dry-powder inhalers require a higher peak inspiratory flow than MDIs for effective drug delivery. Many elderly patients with mild and moderate COPD are unable to generate adequate peak inspiratory flows for optimum use of some popular dry-powder inhalers.

Another common issue encountered in the elderly is cognitive impairment and ability to use inhalers correctly. Not surprisingly, elderly people with significant cognitive impairment were unable to learn to use a standard MDI. Patients with mild-to-moderate dementia may be able to use either an inhaler with a spacer device or an inspiration-triggered inhaler. However, only those patients who had no cognitive impairment were able to demonstrate perfect inhaler technique. Subsequent studies have shown that patients with a Mini-Mental State Examination (MMSE) test score of less than 23 out of 30 or the inability to copy intersecting pentagons are unlikely to master MDI technique. Executive domains are important determinants of an adequate inhaler self-administration technique with or without overt cognitive impairment on the MMSE. A majority of this research has been conducted in a frail elderly population during hospitalizations for rehabilitation, and additional research has been called for in a community-based sample.

In addition to cognitive impairment, patients having difficulties with exhalation, hand-breath coordination, and breath-holding are likely to have difficulty with any inhaler; therefore, frailty may be a central issue. A patient's cognitive function should be assessed prior to initiating therapy with an inhaler to establish a baseline and aid in the selection of an inhaler device. It is not known whether patients with mild-to-moderate dementia can retain inhaler skills as their cognitive function declines. Therefore, planned regular review of technique should take place to test competence and changes made to therapy as necessary. Furthermore, supervision of inhaler use is recommended for patients with cognitive impairment.

It is a myth that nebulizers are more effective than correctly administered inhalers. An evidence-based review of effectiveness reported that nebulizers, DPIs, and MDIs have comparable effectiveness when used properly. The appropriate use of nebulizers does contain complexities, such as the need to disassemble, wash, dry, and reassemble the nebulizer between treatments. Nebulizer compressors require periodic maintenance, such as filter replacement. Subjectively, older adults often seem to prefer nebulizers. Perhaps this is due to the sensation of the taste and sight of the mist; however, no objective evidence has been published to support this notion, and patient compliance with home nebulizer therapy in COPD patients averaged 57% in one study. Appropriate candidates for nebulizer therapy are those patients with very poor hand-breath coordination, such as those with Parkinson disease or severe osteoarthritis of the hands.

Older adults with COPD are at risk for adverse effects from benzodiazepines. Benzodiazepines can impair respiratory drive in individuals with COPD yet are commonly prescribed to treat insomnia, anxiety, and breathlessness. In a study of 111,445 older adults with COPD, almost one third received a new prescription for a benzodiazepine, with higher rates in those with more severe COPD. Benzodiazepines should be used as a second-line treatment for patients with COPD, and the lowest possible dose should be prescribed for the shortest period of time.

Older adults are more likely to develop adverse reactions to pharmacotherapy while receiving asthma therapy (see Table 8-1); there-
Therefore, it is prudent to provide more intense monitoring.26 Most elderly patients will require continuous treatment programs to control their disease. In part, this may be because bronchodilator response to inhaled beta agonists declines with age.27 Even in mild disease, older adults should receive regular preventive treatment with ICS, given the poor perception of bronchoconstriction by older asthmatic patients.28 If symptoms persist despite ICS, the addition of a LABA should be considered. Due to concerns about the safety of beta-2 agonists in older adults, LABA should only be used concomitantly with ICS, and these patients should have regular cardiac assessments, including periodic electrolyte monitoring to rule out hypokalemia.

A critical component of self-management is the provision of a written asthma plan that instructs patients on how to deal with changes in asthma symptoms. In a study that investigated the risk factors associated with hospitalization for asthma, 40% of elderly people with asthma reported that they did not know everything they needed to know to manage flare-ups, adjust their medications, or avoid asthma triggers.5 Most did not have a peak-flow meter, and of those who did, 29% did not know what to do in case of an abnormal reading. It is imperative that written asthma plans and adequate peak-flow counseling are provided to older adults with asthma. If cognitive impairment is present, caregivers should be educated on the steps needed to adjust therapy and when to seek help.

Adverse effects from beta agonists may occur more frequently in elderly patients, especially in those with pre-existing cardiac disease. Levalbuterol, the R-isomer of albuterol, has been touted as producing fewer adverse effects and superior bronchodilation when compared to albuterol. Studies in asthma and COPD have shown mixed results. If an elderly patient has minimal response to albuterol or significant adverse effects, levalbuterol may be considered as an alternative. However, current evidence does not support routine use of levalbuterol as the beta agonist of choice in the elderly.

Inhaled anticholinergic medications may increase intraocular pressure and have other adverse ocular effects. This is important in the elderly population because of the high prevalence of glaucoma, macular degeneration, and other ophthalmologic problems. Several case reports have correlated the use of a loose-fitting mask while administering ipratropium bromide to anisocoria, due to unilateral mydriasis.29 Prolonged pupillary dilation can occur if the drug is sprayed directly into the eye, and this is especially worrisome regarding tiotropium because of its prolonged duration of action. Avoiding contact with the eyes seems to be the best strategy; studies of ipratropium given at four times the recommended dose in patients with normal angle glaucoma had no effect on intraocular pressure, pupil dilation, or accommodation.30

Inhaled anticholinergic medication is poorly absorbed, making systemic side effects unlikely. The most common adverse effect with inhaled anticholinergic medications is dry mouth, but this rarely leads to discontinuation. Inhaled anticholinergic agents have a relatively low incidence of cardiovascular or respiratory adverse effects, although supraventricular tachycardias, increased cardiovascular risk, and paradoxical bronchoconstriction have been reported.6 This notion was challenged recently in a systematic review and meta-analysis of patients using ipratropium or tiotropium, which showed an increased risk for cardiovascular events.31 The analysis included 17 trials that lasted from 6 weeks to 5 years, with nearly 15,000 patients. Patients treated with inhaled anticholinergics were more likely to reach the primary endpoint of cardiovascular death, myocardial infarction, and stroke (1.8% versus 1.2%). When the studies were analyzed based on length, the risk remained elevated in the long-term studies, and short-term studies did not reach statistical significance. These findings remind the clinician to carefully monitor COPD patients receiving long-term inhaled anticholinergic therapy.
Theophylline is generally avoided in the elderly due to its narrow therapeutic index and potential to cause major systemic side effects and drug interactions (see Table 8-1). If theophylline must be used in elderly patients, serum concentrations should be monitored and a lower therapeutic range of 8–12 mg/L should be targeted.32

Tuberculosis

**Etiology, Epidemiology, and Clinical Presentation Specific to Geriatrics**

TB, caused by *Mycobacterium tuberculosis*, has been declining in recent years in the United States due to increased awareness and selective prevention therapy, including treatment of latent infection. The elderly have the highest case reports among all age groups.33 Disease in the elderly mostly occurs in community-dwelling individuals; however, patients who reside in nursing homes and long-term care facilities (LTCFs) are at a 2–3 times higher risk for TB.34,35 Furthermore, the rate of tuberculin reactivity is associated with the length of stay in a nursing home, and in nursing homes with known recent infectious cases.34,35

Elderly patients are at higher risk for TB infection due to higher rates of exposure and infection that occurred early in the 20th century. The increasing likelihood of latent infection combined with immunosenescence increases the likelihood of reactivation. Reactivation of a primary infection in the elderly accounts for 90% of TB, of which a component is from use of newer biologic immunomodulating drugs.34,35 Despite improvements, prevention and control of TB in the elderly population remains a challenge.

The tuberculin skin test (TST) is used to diagnose *M. tuberculosis* infection. It contains a 5-tuberculin unit dose of purified protein derivatives (PPD) injected intradermally to form a weal. Interpretation of TST results 48–72 hours after administration should be stratified according to risk groups. Patients who do not have signs or symptoms of TB but have a positive TST may have latent TB infection (LTBI). Elderly patients may not be able to mount an immune response to provide a positive result to the TST. Therefore, a two-step TST is recommended. If the patient's first TST is negative, a second TST should be given 1–3 weeks later. A positive TST, regardless of whether it was the first or a two-step, warrants a chest radiograph and further investigation to determine treatment modality.

Although relatively uncommon, a false-positive TST can occur, especially in patients who have recently received the Bacillus Calmette-Guérin (BCG) vaccine or those infected with atypical mycobacteria. BCG is not used in the United States. However, foreign-born individuals may have received the BCG vaccine. Cell-mediated immunity to PPD declines over time in individuals who have received the BCG vaccine.34,35 Older patients with a positive TST result should be treated for LTBI or *M. tuberculosis* infection, regardless of whether a history of BCG vaccine is noted in the patient's chart, especially in individuals that came from endemic areas of TB or have been exposed to TB.34,35

LTBI may not be detected in the elderly population because of an inability to mount an immune response to the PPD. A false-negative TST occurs in patients with febrile illness, human immunodeficiency virus (HIV), and other viral disease and in patients taking corticosteroids or other immunosuppressive drugs.34,35 The rate of false-negative in the elderly is more common than in the general population.33 In the elderly, lack of a reaction to TST cannot conclusively rule out TB disease or infection.

**Summary of Standard Treatment in the General Adult Population**

The American Thoracic Society, Centers for Disease Control and Prevention, and Infectious Diseases Society of America have developed treatment recommendations for TB.33 Control of TB is focused on breaking the chain of transmis-
This can be achieved in the United States by (1) rapid detection of TB, (2) screening of high-risk groups, (3) effective treatment of LTBI and active TB, and (4) prevention of TB transmission into the community. The standard treatment for LTBI is isoniazid for 9 months; alternatively, it is a combination of isoniazid and rifapentine given weekly for 12 weeks. Directly Observed Therapy (DOT) can be used. In patients who are intolerant or resistant of isoniazid, daily rifampin can be used for 4 months. For the treatment of active TB, all appropriate specimens should be obtained before empiric therapy is started. DOT and therapy that covers multidrug-resistant TB based on local resistance patterns is recommended. Baseline and monthly monitoring of liver function tests (LFTs) are recommended for individuals with HIV and chronic liver disease.

**Review of Evidence Base Supporting Treatment Recommendations for Elderly Patients**

Recommendations for TB treatment do not differ between adults and the elderly population, according to guidelines. Studies have not focused on the elderly specifically; however, comorbidities and social issues may require adjustments to be made in standard treatment plans. The majority of TB cases in elderly patients in Western societies are probably treatment-sensitive; most infections in the elderly are due to reactivation of disease that was acquired prior to the availability of antituberculous therapy early in the 20th century. The most challenging component in treating elderly patients is selecting the highest effective treatment regimen while diminishing the probability of major adverse reactions. Table 8-3 reviews the common agents used in TB.

**Common Problems Encountered When Treating Elderly Patients with Tuberculosis**

Despite elderly individuals having the highest rate of infection, some view TB as a problem of the young. This, in part, is due to the emergence and focus on HIV-associated TB that predominately occurs in younger individuals. Also, healthcare professionals may not always identify a possible TB infection, because symptoms may be less pronounced, nonspecific, or confused with other pulmonary, heart, or malignant disease; radiological findings may be atypical; and the frequency of false-negative TST occurs more often in the elderly population. These factors contribute to a possible delay in diagnosis, which can result in a higher rate of mortality and the spread of TB.

Anti-tumor necrosis factor (TNF)-alpha treatment has been identified as a risk factor for reactivation of TB in older adults. These biologic immunomodulating drugs are growing in usage for adults of all ages. Studies have been published using an active-surveillance database and the FDA’s Adverse Event Reporting System, which indicate that treatment with infliximab or etanercept is associated with a fivefold overall increased risk of TB. Based on these findings, it is recommended to screen all patients for LTBI or active disease before starting anti-TNF-alpha treatment.

Some LTCFs are reluctant to admit residents with a diagnosis of TB because of the difficulty treating elderly patients successfully and fear of increasing the risk of transmission to other residents. The need for respiratory precautions, resident isolation, equipment dedicated to the patient with TB, and segregated laundry requirements increases the burden on both the facility and staff. For elderly patients newly admitted to a LTCF or nursing home, screening with two-step TST and treatment for LTBI per established guidelines is recommended. Hepatic toxicity with isoniazid has a higher incidence in individuals over 35, and this was a main reason for restricting treatment for LTBI in the elderly in the past when alternative agents were considered first-line for older patients. Intolerance to INH has been documented in older individuals, and the risk for INH-hepatitis is the highest in individuals ≥50 years (2.3% risk). In patients at high risk for hepatotoxicity—those with HIV and chronic liver disease—it is recom-
mended to perform baseline and monthly LFT. Currently, INH is considered first-line therapy in older adults, but symptomatic monitoring of INH-induced hepatitis may not be optimal in elderly individuals with impaired communication or cognition skills or chronic comorbidities. Therefore, it may also be appropriate to monitor LFTs in these patients.

All agents used in treatment of TB have significant toxicities and drug interactions of importance in older adults. Elderly patients, in particular those with diabetes, uremia, malnutrition, or history of alcohol abuse are at higher risk for peripheral neuropathy from INH. To prevent peripheral neuropathy, pyridoxine 25–50 mg/day may be given. INH has also been shown to increase serum concentrations of some benzodiazepines and anticonvulsants. See Table 8-3.

Use of rifampin with pyrazinamide for the treatment of LTBI is strongly discouraged due to the potential for severe hepatotoxicity (see Table 8-3). A complete medication review for potential drug interactions should be completed prior to initiating therapy and concomitant use of known hepatotoxic agents should be avoided.

<table>
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<th>Class: Medication Examples</th>
<th>General Adult Treatment Principles</th>
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<td>Isonicotinic acids:</td>
<td>First-line treatment as monotherapy for LTBI or in combination for active TB.</td>
<td>Monitor liver function and counsel patient on alcohol consumption. Supplement with pyridoxine 25–50 mg/day to prevent peripheral neuropathy. Monitor for drug interactions. May increase concentration of phenytoin, carbamazepine, warfarin, diazepam; corticosteroids may decrease levels of isoniazid.</td>
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<td>Isoniazid</td>
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<td>Rifamycins:</td>
<td>First-line treatment as monotherapy for LTBI or in combination for active TB.</td>
<td>May turn urine reddish/orange. Monitor liver function and counsel patient on alcohol consumption. Monitor for drug interactions. Rifampin may decrease concentrations of methadone, digitalis glycosides, cyclosporine, warfarin, oral hypoglycemic drugs, corticosteroids, theophylline, phenytoin, ketoconazole, protease inhibitors, and non-nucleoside reverse transcriptase inhibitors.</td>
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<td>Rifampin</td>
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*Not a complete list of drug interactions; it is important to screen all medications for drug interactions carefully.*
Case 1: Asthma

Setting:
Skilled nursing facility.

Subjective:
MD is an 82-year-old woman who has been a long-time resident of the skilled nursing facility. Recently, the nursing staff has noted that she is having increasing shortness of breath and nighttime awakenings, which they attribute to a worsening of her asthma.

Past Medical History:
Late-onset asthma, osteoarthritis, hypertension, recently diagnosed glaucoma, and depression.

Medications:
Fluticasone 250 mcg/salmeterol 50 mcg inhaler 1 inhalation BID, albuterol 0.083% solution 3 mL via nebulizer four times a day prn, acetaminophen 500 mg four times a day, furosemide 20 mg daily, metoprolol 50 mg BID, sertraline 50 mg daily. There is an order for timolol 0.5% ophthalmic solution 1 gtt BID, initiated 2 weeks ago.

Allergies:
NKDA.

Social History:
Negative for tobacco and alcohol use.

Family History:
Mother died of old age, father died of a myocardial infarction at age 81.

Objective:
Ht 5’2˝, Wt 101 lb, BP 130/82, P 62 BPM, RR 20

Physical Examination:
Bilateral wheezing, use of accessory muscles on inhalation, remainder of examination is within normal limits.

Assessment:
MD is experiencing shortness of breath caused by bronchoconstriction induced by ophthalmic and systemic beta blockade.

Plan:
1. Recommend the discontinuation of the timolol ophthalmic solution and substitution of latanoprost eye drops.
2. Recommend the discontinuation of metoprolol and substitution of amlodipine 5 mg daily.
3. Reinforce proper inhaler technique with the patient and nursing staff.

Rationale:
1. The use of ophthalmic beta blockers has been shown to exacerbate reactive airway disease because of systemic absorption. Patients already taking systemic beta blockers are at an increased risk for bronchoconstriction, and addition of the topical agent is likely tipping MD into bronchoconstriction. The use of ophthalmic beta blockers should be avoided in patients with a history of asthma. If they must be used, nasolacrimal pressure should be applied for 1 minute after the instillation of the drops to minimize systemic absorption.
2. MD has no compelling indications for the use of a beta blocker (e.g., post myocardial infarction) and has a relative contraindication (i.e., asthma). Amlodipine will not cause bronchoconstriction. The dose should be titrated to achieve blood pressure goal.

3. Proper inhaler technique is difficult to achieve for many elderly patients, and periodic assessment of a patient’s technique is useful to ensure optimal medication management. Because nursing staff are involved in drug administration in LTCFs, they are helpful in evaluating and reinforcing proper technique on a day-to-day basis.

**Case Summary:**

Older adults are at increased risk for adverse drug reactions and drug-induced disease. A careful assessment should be conducted before prescribing any new medications to ensure that the proposed therapy will not exacerbate other chronic conditions. It is imperative that clinicians consider any symptom in an elderly patient a medication adverse event until proven otherwise. Using this mindset, the clinician will not overlook the possibility that the patient may be suffering from a medication adverse event as opposed to worsening of the underlying asthma. Patient education is critical for effective management of asthma and other respiratory disorders. Experts have stated that management of respiratory disorders is 10% medication and 90% education. Patients need to be assessed for their ability to comprehend self-management plans and the complexities of using inhaler devices.
CASE 2: CHRONIC OBSTRUCTIVE PULMONARY DISEASE

Setting:
Assisted living facility.

Subjective:
SM is a 69-year-old male who is a long-time resident of the assisted living facility. Recently, he has been more short of breath. The staff reports that he is having trouble using his inhalers.

Past Medical History:
Parkinson disease ×10 years, COPD, and osteoarthritis.

Medications:
Carbidopa/levodopa 25/250 four times a day, tiotropium inhaler daily, albuterol inhaler four times a day.

Allergies:
NKDA.

Social History:
Denies use of tobacco or illicit drug use; drinks alcohol on special occasions.

Family History:
Lives in assisted living facility, widowed ×5 years.

Objective:
BP 128/78, P 88 BPM, RR 20, Ht 70˝, Wt 205 lb

Physical Examination:
Well-nourished male who is slightly short of breath. Parkinsonian tremor and rigidity noted to both upper extremities R>L.

Assessment:
SM is experiencing shortness of breath that is exacerbated by poor inhaler technique.

Plan:
1. Stop the albuterol and tiotropium inhalers.
2. Start albuterol and ipratropium inhalation solution via nebulizer four times a day.
3. Have staff assist with daily cleaning of the nebulizer

Rationale:
It is likely that his Parkinson disease is interfering with his hand-breath coordination, resulting in less-than-optimal delivery of his bronchodilators. Nebulizers are not dependent on hand-breath coordination and are a better option for this patient.

Case Summary:
It is important for the clinician to determine the best device for administration of respiratory medications. A complete assessment of the physical and mental status of the patient is essential at baseline and periodically thereafter.
Chapter Summary

Respiratory disorders have a significant impact on the quality of life of older adults. Whether it is a chronic condition such as asthma or COPD or an episode of TB, the central issues remain: accurate diagnosis, appropriate therapy, and adequate monitoring. The diagnosis of respiratory disorders in older adults is sometimes challenging due to differences in disease presentation, such as pneumonia and TB. Under-diagnosis is also common in asthma. Regardless of the condition, data evaluating the treatment options for respiratory disorders in older adults are sparse, particularly the frail elderly. In a majority of the cases, the application and adaptation of standard adult treatment will be appropriate. However, the clinician needs to anticipate the various problems that may occur in older adults, including the potential for medication adverse effects, especially in those patients with multiple medical comorbidities; drug interactions in patients receiving polypharmacy; and issues of effective medication delivery, particularly inhaled medications. With appropriate assessment, monitoring, and follow-up, respiratory disorders can be effectively managed in older adults.

Self-Assessment Questions

1. How well are older adults with asthma and COPD represented in the medical literature? What age groups are represented? What medical comorbidities do they have?

2. How can mental status influence the use of inhaled medications?

3. What are the pros and cons of inhalers and nebulizers?

4. What classes of medications should be avoided in older adults with COPD?

5. What is the two-step tuberculin skin test, and why is it useful in older adults?

6. What potential medication-related problems are anticipated with the use of antituberculous drugs?

7. What parameters should be monitored with antituberculous drugs to determine efficacy and safety?
REFERENCES


LEARNING OBJECTIVES

1. Evaluate the changes in renal function that occur with age and determine how these changes result in an increased risk for older patients with chronic illnesses.

2. In a patient with chronic kidney disease (CKD) and diabetes, develop a treatment plan to help preserve renal function.

3. Assess a pharmacotherapy regimen for recent onset drug-induced incontinence in an older person.

4. Distinguish between older men with benign prostatic hyperplasia (BPH) who would benefit from single-agent versus combined therapy with alpha reductase inhibition and alpha blockade.

KEY TERMS AND DEFINITIONS

ARGININE VASOPRESSIN (AVP): A hormone secreted from the posterior pituitary gland that helps to retain water by increasing water absorption in the collecting ducts of the nephron. Vasopressin is also frequently referred to as anti-diuretic hormone (ADH).

DETRUSOR MUSCLE: The muscular coat of the urinary bladder that contracts to empty urine.

KEGEL EXERCISES: Pelvic muscle exercises intended to strengthen the muscles of the pelvic floor to improve urethral and rectal sphincter function.

MICTURITION: Urination or voiding.

NEUROGENIC BLADDER: Dysfunction of the bladder caused by neurologic damage. Potential causes include brain or spinal cord injuries, diabetes, acute infection, or genetic nerve complications.
Renal Disorders

Changes in the Kidney with Age

The aging kidney gradually develops anatomic and physiologic changes that are usually not perceptible until an illness alters the body's compensatory balance. The vascular system changes in the aging kidney, leading to hypertrophy of arteries, with the most significant impact occurring in the cortex of the kidney. Most of the size changes in the aging kidney occur in the cortex with a loss of about 35% of the number of glomeruli as well as a decrease in the surface area and a thickening of the basement membrane of the glomeruli. Glomerular atrophy in the aging kidney results in a decrease of the glomerular filtration rate (GFR) of about 0.75–1.0 mL/min/1.73 m² each year beginning by about 40 years of age. These changes in the structure and function of the kidney in an older person also affect his or her ability to maintain a normal fluid and electrolyte balance, especially when challenged with drugs and illness. Older people experience a delay in compensation to a very low sodium diet as well as an exaggerated increase in blood pressure in response to an increase in sodium intake. Older people also have a decreased response to the diuretic and natriuretic effects of loop diuretics. The regulation of water balance changes with age due to the decreased ability of the aging kidney to concentrate, as well as a decreased ability to excrete a water load. Older people increase their body proportion of fat and lose a similar proportion of water, which leads to greater changes in solutes (such as sodium) and in the clinical consequence of dehydration or fluid overload. These changes in kidney size and physiology result in significant alterations to kidney function with age, resulting in a decrease in GFR and a decreased ability to respond to changes in fluid and electrolyte balance.1,2

Epidemiology and Risk Factors of Chronic Kidney Disease

CKD is a common and important disorder in older persons and is associated with serious adverse outcomes such as kidney failure, cardiovascular disease, anemia, functional decline, and death. In 2002, The National Kidney Foundation defined CKD as the presence of protein (albumin) in the urine for at least 3 months, or an estimated glomerular filtration rate (GFR) of <60 mL/min/1.73 m². This group also created a five-stage system to categorize the severity of renal dysfunction.3 A national data system collects and analyzes information about chronic and end-stage kidney disease, and this information shows that the prevalence of CKD is estimated to be between 14% and 18% of the general population and to be more than 35% in people who are over the age of 60 years. In addition, of those individuals who have progressed to end-stage renal disease, 20% are between the ages of 65 and 74 and 16% are 75 years of age or older. As the prevalence of kidney disease continues to be collected by the National Kidney Foundation, rates of end-stage renal disease have stabilized for middle-aged individuals but have increased for those in the older age groups.4

The National Kidney Foundation recommends evaluation of patients on the basis of their risk factors, initiation factors, and progression factors.3 One of the most important risk factors that contributes to the development of CKD is advanced age. Initiation factors are diseases that cause renal damage and include diabetes and hypertension, two diseases that are strongly associated with age. Progression factors accelerate the damage to the kidney and include hyperglycemia, hypertension, and proteinuria. Other progression factors that can be modified include smoking, hyperlipidemia, and obesity. Progression factors occur commonly in older individuals and are potentially modifiable by medication therapy management.3

Disease Progression in the Elderly

The natural course or progression of CKD to end-stage renal disease is different between younger and older people. CKD progresses in association with factors such as proteinuria, hypertension, diabetes, smoking cigarettes, hyperlipidemia, and obesity. The effect of age
on the progression of CKD was evaluated in a large cohort of elderly veterans, with kidney disease showing an expected inverse relationship between estimated GFR and rates of end-stage renal disease and death. In the older men with initial moderate kidney disease, the percentage who experienced a further decrease in GFR each year increased with age. For men with moderately severe disease, the percentage of men who further decreased their GFR was less with age. The older men with more severe kidney disease were more likely to die than progress to end-stage renal disease. This research suggests that older age is a strong modifier of disease course, with more rapid progression from moderate to moderately severe disease and less progression of moderately severe disease to end-stage disease. This difference in progression may be due to greater disease comorbidity in older men that leads to death, to a stabilization of moderate kidney disease in older persons, or perhaps to a difference in the underlying cause of kidney dysfunction in the elderly.

**Diagnosis of Chronic Kidney Disease in the Elderly**

Renal function, as defined by GFR, declines with age by approximately 0.75–1.0 mL/min/1.73 m² each year beginning by about 40 years of age. Identification of CKD in older persons is important for several reasons. Individuals with an estimated GFR of ≤60 mL/min need to have adjustments of the doses of renally eliminated medications. Prevention of end-stage renal disease can become a focus of medication therapy management if CKD is documented. Frequently, CKD occurs in older patients with diabetes and or hypertension, which highlights the importance of achievement of goal treatment values in the management of these two chronic diseases. Pharmacists who participate in medication therapy management are uniquely situated to help older people achieve goal treatment values for chronic diseases, which can slow progression of CKD.

**Estimation of Renal Function**

There is some controversy about the preferred method for estimation of GFR in older people. To estimate GFR, the serum concentration of an endogenous filtration marker, such as creatinine, is measured and the clearance of creatinine is computed with a mathematical formula. The mathematical equations have been developed from patient studies that use regression formulas to correlate the serum level of creatinine to the measured GFR. Often, patient factors are included in the formula such as age, body weight, and sex to improve the correlation between measured and estimated GFR. Chapter 3 discusses the specific formulae employed for estimating GFR and the pros and cons of each, but, in general, it is the Cockcroft-Gault equation that is used to estimate renal function for the purposes of determining the renal dose adjustment of medications. The four-variable Modification of Diet in Renal Disease (MDRD) equation, which adjusts for age, sex, creatinine, and race, yields an estimate of GFR and is used to stage patients with CKD.

**KEY POINT:** Estimation of GFR through the use of the MDRD and estimation of creatinine clearance through the Cockcroft-Gault equation should both be performed for older patients as a part of a comprehensive medical and pharmaceutical assessment.

**Treatment of Chronic Kidney Disease**

The goals of treatment for all ages of people with CKD are to delay or prevent the progression to more severe stages of disease, including end-stage renal disease, and to prevent the occurrence of complications related to CKD. However, because older patients generally have multiple chronic diseases and are more likely to die with kidney disease rather than from kidney disease than younger individuals, interventions should be tailored to meet the patient’s lifestyle prefer-
ences, to maintain optimal physical and mental functioning, and to maintain quality of life. Interventions include nonpharmacologic (dietary protein restriction) and pharmacologic. Drug therapy recommendations may be different for those with diabetic CKD than for those with CKD because of other causes.

Dietary restriction of protein in amounts up to 0.6 g/kg per day is recommended by the National Kidney Foundation for individuals with a GFR <25/mL/min/1.73 m². The literature that supports this recommendation is inconsistent and suggests that a reduction in rate of decline of the GFR is small at 0.5 mL/min per year. Dietary protein restriction has not been specifically evaluated for efficacy or safety in older people. Given that the benefits are small and the risks for malnutrition and changes in quality of life with protein restriction are significant, intake levels of up to 0.75 g/kg/day are reasonable for older people.9

**Pharmacologic Therapy**

To prevent progression of CKD, drug therapy is specifically targeted toward control of the underlying disease that initiated the kidney disease, generally either diabetes and/or hypertension. Diabetes and hypertension both initiate CKD as well as contribute to disease progression. A comprehensive approach to the medical management of older patients with diabetes, hypertension, and renal diseases is vital.

**Glycemic Control to Prevent Chronic Kidney Disease in an Older Patient with Diabetes**

In older patients with type 2 diabetes, intensive therapy that achieves goal HbA₁c values of ≤7.0% substantially reduces albuminuria,10-12 but with the risk of more frequent hypoglycemic reactions.13,14 Clinical practice guidelines have summarized the strong evidence that exists between HbA₁c and the emergence of albuminuria, although the evidence that links glycemic improvement to a prevention of decline of the GFR is weaker.15 Two important publications highlight both the risks and efficacy of intensive therapy in older patients. More than 11,000 patients with type 2 diabetes, who were 66 ± 6 years of age (mean ± standard deviation) were randomized to receive intensive therapy to achieve HbA₁c values ≤6.5% or to standard therapy where the HbA₁c values were generally between 7% and 8%.13 This cohort represents the younger end of the age range referred to as elderly. Frail individuals of very advanced age or with multiple comorbidities, disability, or dementia were not well represented. All patients were treated with multiple oral agents that most often included a sulfonylurea with metformin. Patients in the intensive arm of the study received a modified formulation of gliclazide and were more likely to be treated with insulin than the standard treatment group (40% versus 24%, respectively). After five years of treatment, patients in the intensive arm of this study had a reduction by one-fifth of new or worsening nephropathy. Rates of hypoglycemia were higher in the intensive versus standard treated patients (2.7% versus 1.5%, respectively).13 For older patients with type 2 diabetes, the risk of hypoglycemia was even higher, with an even more aggressive glycemic goal regimen (HbA₁c <6%) versus standard management (HbA₁c between 7% and 7.9%), resulting in significantly more deaths in the aggressive treatment arm.14

Older patients are more likely to experience hypoglycemia, which may be due to their underlying renal disease with a decreased ability to eliminate both insulin and oral antidiabetic drugs. Furthermore, patients with kidney disease have decreased renal gluconeogenesis, which reduces an important compensatory response to counter hypoglycemia.15,16 Due to these limitations, glipizide is the preferred sulfonylurea for use in older patients with kidney disease because the drug is metabolized to inactive compounds.17 Metformin is recommended as an effective and preferred beginning therapy for patients with type 2 diabetes due to its broad range of benefits and lack of hypoglycemia.18 Use of metformin may be limited in older people due to prescribing guidelines that recommend individuals need adequate renal function to clear
this drug and prevent lactic acidosis.

In addition to recommendations to avoid metformin with serum creatinine >1.4 mg/dL in women and 1.5 mg/dL in men, creatinine clearance should also be considered. Official product information recommends a minimum creatinine clearance of >60 mL/min, although there are some data that suggest metformin can be used in individuals with creatinine clearance as low as 30 mL/min.\textsuperscript{18,19} Although age >80 years is not an absolute contraindication for use, caution is required due to the increasing likelihood of insufficient renal function with advancing age. Other oral agents that may be preferable for use in patients with impaired renal function include repaglinide, a nonsulfonylurea secretogogue. This class of oral agents is shorter acting and lowers postprandial glucose more than fasting glucose concentrations, which results in less hypoglycemia. Pioglitazone may also be the preferred thiazolidinedione for use in the elderly with renal insufficiency, although concerns about weight gain and fluid retention with this class of medications warrants careful monitoring.\textsuperscript{15-17}

Based on the evidence that tight glycemic control is associated with hypoglycemia that doesn’t improve overall health outcomes for people with comorbidities or limited life expectancy, the 2012 guideline updates recommend an HbA\textsubscript{1c} concentration in the 7% to 8% range.\textsuperscript{15,17}

**Control of Cardiovascular Risk Factors in Older Patients with Chronic Kidney Disease**

The Eighth Joint National Committee (JNC 8) guidelines suggest the appropriate blood pressure goal for people with CKD is <140/90 mmHg.\textsuperscript{16} Specific drug recommendations from the JNC 8 guidelines are reviewed in Chapter 7. In general, the use of either an angiotensin-converting enzyme (ACE) inhibitor or angiotensin receptor blocker (ARB) as first-line therapy to treat hypertension or proteinuria in patients with CKD is advised. Although the long-term outcomes of this type of drug therapy intervention is less clear in very frail individuals, the prevention of further renal compromise is important to preventing future morbidity among younger groups of the geriatric population. There are generally no significant age-related pharmacokinetic or pharmacodynamic differences between older and younger patients in the use of ACE inhibitors or ARBs.\textsuperscript{20}

To avoid renal toxicity in patients who may be volume depleted from diuretics or for those also receiving nonsteroidal anti-inflammatory drugs, ACE inhibitors and ARBs should be started at low dosages and slowly titrated to effect. For those at high risk of renal toxicity, the diuretic or nonsteroidal anti-inflammatory agent can be held for 2–3 days to prevent an acute decline in renal function related to any underlying dehydration.\textsuperscript{20} ARBs may cause fewer side effects, such as cough and angioedema, and can be used as alternatives to ACE inhibitors. The combined use of ACE inhibitors with ARBs is sometimes recommended to prevent renal angiotensin escape, thus providing for a greater effect on blood pressure control and albuminuria.\textsuperscript{20} However, elderly individuals with impaired renal function are at increased risk for hyperkalemia with these medications, and for this reason ACE inhibitors are often cited among the classes of medications with a high prevalence of adverse effects in the long-term care setting. Increased monitoring of serum potassium may be required for individuals receiving medications that alter serum potassium, such as potassium supplements, potassium-sparing diuretics, ACE inhibitors, and ARBs.

Hyperlipidemia increases albuminuria, which accelerates the progression of CKD. In addition, death from atherosclerotic causes is high in patients with CKD. The 2012 Kidney Disease Outcomes Quality Initiative (KDOQI) updates recommend treatment of patients with CKD with an HMG-CoA reductase inhibitor (statin).\textsuperscript{15} However, the 2013 American College of Cardiology/American Heart Association Blood Cholesterol Guidelines do not specifically identify patients with CKD for treatment with statins. The guidelines do recommend moderate-intensity statin therapy in patients with CKD who also have clinical atherosclerotic cardiovascular
there is very little information available about age-related changes in either the pharmacokinetics or pharmacodynamics with the use of statins. Almost all clinical trials with statins for the prevention of adverse health consequences from hyperlipidemia have included at least some older individuals, with results supporting treatment. This research includes individuals who are in their 60s and 70s but generally does not evaluate individuals in their 80s and 90s. Because the risk of statin-associated myopathy is higher in older patients receiving moderate to high doses of statins, caution is advised when using higher doses in older people. Even though there are differences in the two guideline recommendations with respect to the use of statins in patients with CKD, it is unlikely to yield differences in treatment because almost all older patients with CKD have comorbidities such as diabetes and/or atherosclerotic cardiovascular disease.

The management of other complications related to CKD, such as anemia and bone disease, is especially important in older people. As the GFR decreases, erythropoietin secretion diminishes, causing anemia of CKD. This complication and its treatment are covered in Chapter 16. Phosphate excretion decreases with worsening renal disease, leading to an increase in serum phosphorus, a decrease in serum calcium, a decrease in vitamin D activation, hyperparathyroidism, and an increase in calcium resorption from bone. These adverse effects on bone add further risks of bone disease and fracture to the older person who may already have coexisting osteoporosis. In this setting, serum phosphorus, calcium, and vitamin D₂ concentrations should be measured so that appropriate supplementation can occur. Phosphate binders are needed as the first step in controlling this problem, although an ideal formulation or regimen does not exist. Calcium-containing products are often used to bind phosphate and can be taken with meals in doses that are often associated with side effects such as nausea, vomiting, and constipation. These regimens may also add to the pill burden in an older patient’s medication regimen. Sevelamer is a newer noncalcium-based agent that binds to phosphorus in exchange for chloride and can be used as sole therapy or in combination with other phosphate binders. Because sevelamer is a polymer that is not absorbed, older patients should be carefully monitored for constipation to prevent bowel obstruction.

**Fluid and Electrolyte Disorders**

The renal system has a remarkable capacity to adjust to changes in our body from the environment and disease processes. However, the kidney’s ability to adapt and change decreases with age, making older people more susceptible to fluid and electrolyte imbalance. In addition, older people are much more likely to have underlying diseases and drug treatments that place them at further risk for fluid and electrolyte disorders. Due to the changes in the kidney mentioned at the beginning of this chapter, older people have a reduced ability to concentrate their urine as well as a lessened ability to excrete an increased water load. Vasopressin secretion and thirst are the regulators of water balance. Vasopressin levels tend to increase with age as a result of a loss of sensitivity to this hormone by the kidney. Also, older people have a decreased thirst sensation and are more likely to have cognitive impairments that, when coupled with the decreased function of the kidney, place them at great risk for dehydration. Dehydration is a common problem in nursing home residents and is a frequent cause for admission to the hospital. In the community, the elderly are at great risk for dehydration and death, particularly during heat waves in the summer. Because of the loss of total body water with aging, relatively mild dehydration can have significant effects on serum electrolytes. The recognition of this condition is more problematic in the elderly due to diminished skin turgor from age-related effects on the skin, and dry mucus membranes can be present in those who breathe
through their mouth. Autonomic reflexes decline with age, diminishing the vasomotor response to heat.\(^1\) Measurement of serum sodium is an important part of an assessment of hydration status because changes in serum sodium concentration usually reflect either an excess or deficit of water.

**Sodium and Water Imbalance in the Elderly**

Hypernatremia (serum sodium >145 mEq/L) is a hypertonic condition that is usually due to a deficit of water and is most common in the elderly with an impaired thirst sensation and or a lack of access to water. Older patients with dehydration usually present with a change in mental status such as lethargy, increasing confusion, and postural hypotension.\(^1\) Treatment should focus on the repletion of water and sodium at a rate that is slow enough to allow for equilibration of water into the brain. Fluid replacement that is too rapid may cause cerebral edema and brain toxicity, leading to seizures and death.\(^2\,3\) Fluid replacement with intravenous normal saline (or less concentrated solutions) should not exceed approximately 150–200 mL/hr to restore the intravascular volume, and then at slower rates, with half-normal saline solutions, to correct the water deficit.\(^1\,3\) In older persons, hypernatremia and dehydration have often developed gradually; therefore, the correction of this condition should, likewise, be in a slow and cautious manner. Changes in serum sodium should not exceed 6–8 mEq/L over 24 hours.\(^2\,3\) When rehydration therapy is underway, monitoring of the patient is needed. This can include laboratory assessment with serum electrolytes as well as clinical signs of improvement in the patient, such as moistness of mucus membranes, skin turgor, concentration of urine, and mental status.

Hyponatremia (serum sodium <135 mEq/L) is a common disorder and an independent predictor of mortality in community-dwelling and hospitalized older people.\(^1\) Chronic mild hyponatremia in the elderly is associated with an increase in falls, osteoporosis, and bone fractures.\(^1\,2\,4\) Evaluation of data from the National Health and Nutrition Examination Survey (NHANES III) reveals a linear relationship between serum sodium and femoral neck bone mineral density, suggesting that for each 1 mmol/L decrease in serum sodium a loss of 0.037 g/cm\(^2\) in bone mineral density of the femoral neck occurs.\(^2\,5\) In the older person, hyponatremia is usually due to fluid excess, often from an overcorrection of dehydration with isotonic fluid.\(^1\,2\,3\) Evaluation of the serum osmolality will help determine whether or not the patient has an isotonic, hypertonic, or hypotonic variety of hyponatremia. Hypotonic hyponatremia is more common, and further evaluation of the urine sodium concentration will help determine whether the patient is hypovolemic (generally due to thiazide diuretics), hypervol- emic (generally due to congestive heart failure, cirrhosis, or overcorrection with isotonic fluids), or euvoletic (generally due to low sodium intake, polydipsia, or the syndrome of inappropriate ADH secretion).\(^2\,3\) In a patient with hyponatremia, knowledge of the volume status guides therapy.

Thiazide diuretics are a frequent cause of hypotonic hyponatremia because they block sodium reabsorption in the distal tubules of the renal cortex, which increases sodium and water excretion by the kidney. Arginine vasopressin or ADH is released to counter the decrease in plasma volume, which increases the reabsorption of free water, resulting in a hyponatremia that is due to a net loss more of sodium than water.\(^2\,3\)

Treatment of hypovolemic hyponatremia should begin by addressing the cause (such as discontinuation of the thiazide diuretic) and replacement of the sodium and fluid deficit in a manner consistent with the severity of symp- toms in the patient. The sodium deficit can be calculated by subtracting the desired serum sodium value from the patient's observed sodium and multiplying by the patient's total body water. Estimates of total body water for older men equal 0.5 L/kg x weight (kg) and for older women 0.45 L/kg x weight (kg). For example, total body water for an 80-year-old, 60-kg woman is 27 L. If this woman had a serum sodium of 120 mEq/L and a desired value
of 125 mEq/L, her sodium deficit would be 135 mEq \((125 - 120) \times 27\). One liter of normal saline contains 154 mEq of sodium. In patients with severe central nervous system (CNS) symptoms, such as coma or seizures, normal saline in small amounts to slowly raise the serum sodium by 6–8 mEq/L over 24 hours is a treatment goal.\(^2\) Ringer’s lactate may be a preferable replacement solution because normal saline solutions have relatively more chloride in comparison to the plasma and may lead to a hyperchloremic acidosis.\(^1\)

For patients with hypervolemic hyponatremia, treatment is focused on achieving a negative water balance by increasing water excretion and limiting oral fluid intake to <1,000 mL/day. If congestive heart failure is the cause for this condition, optimal treatment for the heart failure should be instituted.

Drugs can be a cause of euvolemic hyponatremia. Although the overall incidence of syndrome of inappropriate ADH is relatively low, it is higher in the elderly. In addition, many classes of drug therapy can cause drug-induced syndrome of inappropriate ADH, and drug regimen review is recommended for older individuals with signs of hyponatremia. Commonly reported drug-induced causes include antidepressants (many agents but older women are especially at risk with selective serotonin reuptake inhibitors [SSRIs]), antipsychotics, anticonvulsants, and antineoplastic agents. Drug-induced syndrome of inappropriate ADH secretion has also been reported with analgesics such as fentanyl and ibuprofen, antiparkinson medications, clonidine, ACE inhibitors, amiodarone, and theophylline. Discontinuation of the offending agent is recommended.\(^2\)

Hypomagnesemia occurs with long-term use of proton pump inhibitors due to a reduction in passive absorption of magnesium in the intestines.\(^2\) It is estimated that about one-third of the elderly take proton pump inhibitors, so this adverse drug effect will be more common in the elderly. Low magnesium concentrations are associated with cardiovascular disease and with cardiovascular complications in patients with CKD. Symptoms of mild to moderate hypomagnesemia include muscle cramping, nausea, vomiting, fatigue, and weakness. The use of proton pump inhibitors and magnesium levels was evaluated in a cohort study of elderly people admitted to a hospital over a 6-month period. These individuals averaged 84 years of age; 42% were taking a proton pump inhibitor, and 33% were male. Two-thirds of the study participants had been taking the proton pump inhibitor for longer than 12 months. Elderly participants who were receiving a proton pump inhibitor and who had an estimated GFR of <60 mL/min had magnesium levels that were lower than other comparison groups.\(^2\) Pharmacists should carefully monitor patients for this adverse effect and confirm the need for continued therapy with the proton pump inhibitor.

**Urologic Disorders**

**Urinary Incontinence**

Urinary incontinence (UI) is defined as involuntary urine loss and is a condition that is not always recognized or reported.\(^2\)\(^-\)\(^3\) Individuals may be reticent to self-report UI to their health providers due to embarrassment, yet it can negatively impact dignity and contribute to increased social isolation. Approximately 30% of older adults within the community and almost 60% of individuals residing in long-term care facilities are affected by UI.\(^2\)\(^8\)\(^-\)\(^9\)\(^3\) Although the prevalence of UI increases with age, it is not considered a normal part of aging.\(^2\)\(^8\)\(^-\)\(^9\) The incidence in men is about one third that of women, but at the age of 80, men and women have similar rates of UI.\(^2\)\(^8\)\(^-\)\(^9\)\(^3\) This disorder is expensive, with annual direct costs in the United States approaching $20 billion. An estimated 70% of the cost is due to routine incontinence protective items such as pads, diapers, and skin care products, but the cost of institutional care significantly contributes to this figure.\(^2\)
Before classifying the various types of UI, review of the anatomy and physiology of the aging bladder is needed. The lower urinary tract is composed of the bladder (including the **detrusor muscle**), urethra, urinary sphincter, and nearby musculofascial components including nerves, connective tissue, and blood vessels.\(^{32}\) Urination is controlled by the CNS, the spinal cord, and the peripheral nerves. The parasympathetic nervous system (PNS), the sympathetic nervous system (SNS), and the somatic nervous system all work together to execute proper bladder control.\(^{33}\)

Overall, bladder physiology and **micturition** are regulated by the action of various neurotransmitters and nervous systems (**Figure 9-1**).\(^{33}\) Acetylcholine is the major neurotransmitter responsible for bladder contraction and interacts with muscarinic receptors on the detrusor muscle.\(^{34}\) Of the five known muscarinic subtypes \(M_1-M_5\), \(M_2\) subtypes predominate on the bladder smooth-muscle cholinergic receptors. The \(M_3\) receptors are responsible for both the emptying contraction associated with urination as well as involuntary bladder contractions that can lead to UI. \(M_3\) receptors appear to be the most clinically relevant within the human bladder, and many antimuscarinic drug therapies are targeted at blocking this receptor subtype.\(^{31,34}\) Disturbances in the neural regulation of micturition at any point (pelvic nerves, spinal cord, or brain) may result in UI due to changes in lower tract function.\(^{32}\)

Sensory receptors in the bladder are stimulated as it fills with urine, and signals are sent to the brain indicating bladder fullness. Variability exists within older adults, but approximately 100–200 mL of urine is required before the brain will sense bladder fullness. Stimulation of the SNS and inhibition of the PNS occur during low bladder volume, and this leads to bladder filling

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**Figure 9-1.** Basic bladder anatomy and physiology.  
by contraction of the internal sphincter and relaxation of the detrusor muscle. Inhibitory signals by the brain are replaced by impulses that stimulate the PNS when the bladder is full and micturition is necessary. Detrusor contraction results as well as relaxation of the internal sphincter and inhibition of the SNS. Urinary flow will occur when intravesical pressure is greater than the resistance within the urethra. Once the bladder has emptied and is ready to be filled again, the brain signals parasympathetic inhibition and sympathetic stimulation, resulting in detrusor relaxation and contraction of the internal sphincter.33-35

Specific age-related physiological changes occur within the urinary tract including decreases in bladder elasticity and bladder capacity, as well as more frequent voiding. The detrusor muscle may contract spontaneously; in addition, reduced muscle strength can lead to incomplete bladder emptying. There is also a decrease in the urethral closing pressure and difficulty in postponing urination.28,31,32 Sex-specific changes also occur. Up to 70% of women affected by UI attribute symptom onset with menopause. Women experience a decline in bladder outlet and urethral resistance due to the decreased circulating estrogen levels in the genitourinary tract and the effect on the pelvic musculature. Diminished estrogen levels can lead to atrophic vaginitis and urologic complications including dysuria, urgency, and the development of UTIs. Age-related loss of tone in the muscles of the pelvic floor due to childbirth and/or obesity can also contribute to incontinence. UI is less common in men and carries a later and more sudden onset than in women. Prostate enlargement can lead to decreased urinary flow rates, instability of the detrusor muscle, and overflow incontinence.28,36

UI can be categorized by the duration of symptoms, clinical presentation, or physiologic abnormalities. In addition, transient causes of UI are a special consideration in older adults and should be differentiated from established incontinence secondary to urinary tract dysfunction. The following mnemonic (spells DIAPPERS with an extra “p”) is used to identify some of these reversible causes: delirium, infection, atrophic vaginitis and urethritis, pharmacological agents, psychiatric disorders, excessive urine output, restricted mobility, and stool impaction.30,31 Table 9-1 highlights some of the medication classes often implicated in causing or worsening incontinence.28,32,34,35

Types of Urinary Incontinence
Stress incontinence typically occurs when the urinary sphincter is compromised and no longer

<table>
<thead>
<tr>
<th>Drug Class</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>ACE inhibitor</td>
<td>Occurrence of cough can increase intra-abdominal pressure and aggravate stress incontinence</td>
</tr>
<tr>
<td>Acetylcholinesterase inhibitor</td>
<td>Polyuria, frequency</td>
</tr>
<tr>
<td>α-adrenergic agonist</td>
<td>Increases internal sphincter tone</td>
</tr>
<tr>
<td>α-adrenergic blocker</td>
<td>Decreases internal sphincter tone</td>
</tr>
<tr>
<td>Anticholinergic</td>
<td>Decreases detrusor muscle contraction, possible urinary retention</td>
</tr>
<tr>
<td>Calcium-channel blocker</td>
<td>Decreases detrusor muscle contraction, possible urinary retention</td>
</tr>
<tr>
<td>Diuretic</td>
<td>Increases bladder filling, polyuria</td>
</tr>
<tr>
<td>Opioid</td>
<td>Decreases detrusor muscle contraction; possible urinary retention, fecal impaction, and sedation</td>
</tr>
<tr>
<td>Sedative/hypnotic</td>
<td>Confusion, functional incontinence</td>
</tr>
</tbody>
</table>
able to resist the urine flow from the bladder, especially during physical activity. Transient increases in intra-abdominal pressure can lead to losses of small volumes of urine when laughing, sneezing, coughing, bending, or lifting. This is the most common type of incontinence in women and risk factors include pregnancy, childbirth, menopause, cognitive impairment, age, and obesity. Hormonal factors play a role because the prevalence increases after menopause with estrogen deficiency. Men also can experience stress incontinence, but usually only as a result of internal sphincter damage from urological procedures, including prostate surgery.32-34

Urge urinary incontinence (UUI) and overactive bladder (OAB) are associated with detrusor muscle overactivity. The terms overactive bladder, urge urinary incontinence, and detrusor over-activity are used synonymously at times but need to be differentiated. OAB is a symptom complex that involves urinary urgency with or without UUI, urinary frequency (more than eight voiding episodes in a 24-hour period), and nocturia (two or more nighttime awakenings to void).35 It is important to recognize that OAB can result with or without the features of UUI.33 Individuals with UUI experience detrusor overactivity that leads to forceful, early detrusor contractions before the bladder is full and results in urinary urgency and frequency.34

**KEY POINT:** Detrusor overactivity is a specific diagnosis obtained by urodynamic testing that identifies involuntary detrusor contractions during the filling phase. OAB, in contrast, does not require invasive urodynamic testing and is diagnosed primarily by report of patient symptoms. These terms should not be interchanged, because the definitions are distinct.

The cause of UUI and OAB may either be neurogenic or myogenic, and differing theories exist. The mechanism for the neurogenic hypothesis implies that disease-related changes within the peripheral nervous system or the CNS lead to UUI and OAB. The myogenic hypothesis states that these conditions occur as a result of smooth muscle changes within the bladder wall. In practice, these etiologies are often related, so it is difficult to differentiate.32,35

Overflow incontinence occurs as a result of urethral overactivity and/or bladder underactivity. The bladder is at maximum capacity and distended but is unable to empty, and this leads to the leakage of urine.32,34 Individuals usually present with symptoms of dribbling, weak urinary stream, hesitancy, or incomplete voiding. Causes can be neurogenic, such as diabetes mellitus, spinal cord injuries, or multiple sclerosis. Anticholinergic medications, conditions causing detrusor muscle underactivity, or denervation of the bladder wall musculature are examples of other potential causes. In men, obstructed urinary outflow due to BPH or prostate cancer is another common cause of overflow incontinence and an important consideration.29,34

Individuals with functional incontinence are unable to reach the toilet in time, either due to physical (e.g., impaired mobility, poor vision) or cognitive issues (i.e., dementia, confusion, medication side effects). There are no defects within the urinary tract, related to a primary disease (e.g., dementia, postoperative orthopedic surgery).29

Mixed types of incontinence exist and diagnosis can be confusing because of the overlap of symptoms. The combination of bladder overactivity and urethral sphincter underactivity is one common form of mixed incontinence. Another mixed form characterized by bladder overactivity (instability) and impaired bladder contractility may also occur in elderly men, leading to a mixed condition known as detrusor hyperactivity, with impaired contractility.29,32,36 Signs and symptoms of the mixed conditions are typical of the forms of incontinence that make up the individual diagnoses.
Neurogenic bladder, a type of overflow incontinence, involves the loss of voluntary control of bladder function due to spinal cord injury or neurological conditions. This type of incontinence is managed by intermittent catheterization or placement of a suprapubic tube. Elderly patients may be vulnerable to inappropriate use of catheters for other types of incontinence, which can lead to complications from chronic catheter use.\(^{31}\)

**Treatment**

When treatment options are considered for UI, goals must be identified along with a plan that will be suitable for the individual, whether at home, residing in a long-term care facility, or any other living situation. These goals should target a reduction in the frequency and severity of incontinence episodes and should minimize related complications. Frequently, these complications are overlooked, and clinicians cannot underestimate the importance of weighing the risks and benefits of treatment options. Potential complications of not treating UI include skin breakdown, UTIs, increased risk of falls, sleep disturbances, psychological effects including depression, isolation from activities, and changes in dignity relating to embarrassment.\(^{29-31}\) Treating the underlying cause(s) is desirable but not always an option due to the individual’s overall condition, treatment preferences, and functional ability.\(^{29}\) In some cases, behavioral therapy is appropriate, and nondrug therapies may be the only choice for individuals if drugs or surgery are not desirable. However, multiple pharmacological agents are now available with a variety of mechanisms and profiles that may suit specific needs.

Regardless of the type of UI an individual experiences, it may be necessary to use incontinence undergarments as a means to avoid the soiling of clothing from a wetting episode. For some individuals with occasional or minor symptoms, incontinence shields or adult briefs may be the sole intervention chosen. These products may also be used in combination with drug therapy, because wetting episodes may still occur. In very frail or functionally dependent patients, adult briefs with regular changing and personal cleansing are a mainstay of incontinence care. For those individuals who are dependent on a caregiver for all toileting and personal hygiene activities, especially those with significant cognitive impairment, the decision is often made to discontinue pharmacological intervention for incontinence. If drug therapy does not result in a reduction of wetting episodes, urge discomfort, or the need for adult briefs, the side effect profile may outweigh the benefit in these individuals.

**Nondrug Therapy and Behavioral/Muscle Rehabilitation**

Individuals with OAB or detrusor overactivity often respond to behavioral therapy. According to the American Urological Association, this should be implemented before any pharmacological treatment.\(^{28,37}\) One method focuses on altering bladder function by modifying habits to include delayed voiding. Behavioral training is another approach that targets the bladder outlet; this includes pelvic floor muscle training to improve urge suppression.\(^{37}\) Bladder training is a general term that refers to a combination of patient education, voiding schedules, urge suppression techniques, and pelvic muscle exercises. Toileting assistance protocols are helpful in patients with cognitive or mobility impairment.\(^{35}\) Using routine toileting, prompted voiding, and habit-training schedules will empty the bladder regularly to minimize leaking.\(^{37}\) In addition to OAB and UUI, behavioral techniques are often used for stress and mixed incontinence.\(^{32}\)

Bladder training involving urge control strategies works well in individuals with higher cognition, ability to toilet, and motivation to cooperate with a training program. To retrain bladder habits, scheduled toiletings are adjusted for longer or shorter times, depending on the individual voiding pattern. This may be an option for individuals who are cognitively or physically impaired and need reminders or assistance with the process. Overflow incontinence can also be managed by instructing individuals to void on a regular schedule (i.e., every 2 hours) to avoid increased volume and bladder distention.\(^{29,32,38}\)
Pelvic muscle rehabilitation and exercises can be effective in stress, urge, and mixed incontinence. Examples include biofeedback, vaginal weight training, and Kegel exercises. Most effective in motivated individuals with adequate cognition, proper technique is required to contract the pelvic floor muscles during Kegel exercises without the use of accessory muscles. The exercises strengthen the periurethral and pelvic floor muscles and must be performed regularly to be effective. Kegel exercises or other forms of pelvic floor muscle rehabilitation may be used in combination with bladder training. Several studies in women show the combination to be more effective than either alone. Older adults with cognitive impairment face additional challenges with these techniques. They may require regular reminders to urinate and dryness checks to enhance bladder training. Keeping a bed pan or commode near the bed may also prevent potential falls and subsequent injuries.

**Drug Therapy**

Drug therapy for UI becomes necessary when the symptoms are not sufficiently managed with nonpharmacological therapies. Often, the combination of drug therapy with behavioral or muscle rehabilitation is utilized for optimal results. Pharmacological interventions have the potential to reduce the number of incontinence episodes experienced per day while increasing the volume of urine that the bladder can hold. Medications target specific underlying abnormalities, and it is imperative to identify the type of incontinence before beginning pharmacological treatment. Table 9-2 summarizes possible pharmacologic options for treating various forms of UI. Table 9-2

**Drug Therapy for Stress Incontinence**

There are currently no Food and Drug Administration (FDA)–approved agents to treat stress urinary incontinence (SUI). Alpha-adrenergic agonists such as pseudoephedrine lack selectivity for the urethral alpha adrenoreceptors and cardiovascular safety concerns exist. Imipramine and estrogen are options with limited efficacy. In addition, data from the Heart and Estrogen/Progestin Replacement Study demonstrated an increased risk of stress and urge incontinence in women who were randomly assigned to receive estrogen alone or the combination of estrogen and progesterone compared with placebo. Using oral hormone therapy for the treatment of stress incontinence is generally not recommended; however, the European Association of Urology (EAU) does endorse the use of intravaginal estrogen as a Grade A level recommendation for the improvement of vaginal and urinary symptoms in postmenopausal women. Supporting evidence is based on the fact that besides an improvement in vaginal atrophy, local estrogen therapy may reduce UI and also the frequency and urgency associated with OAB. Local estrogens demonstrated a greater effect than placebo at improving UI and reducing frequency. The EAU recommends to offer topical estrogens to postmenopausal women with UI (stress, mixed, and urgency), although the preferred method of delivery or duration of therapy has not yet been determined.

Duloxetine hydrochloride is a selective reuptake inhibitor of serotonin and norepinephrine. It is not currently approved for SUI in the United States, but it is approved by the regulatory agency in the European Union. In women, it may result in stronger urethral contractions, with an improvement in sphincter tone during urine storage and physical stress. Randomized, placebo-controlled trials of duloxetine have been published demonstrating significant benefits in SUI; however, the emergence of adverse events such as nausea, dry mouth, and fatigue within the trials can be problematic for many healthy, nondepressed individuals. Initial manufacturer recommended doses were poorly tolerated and left clinicians with a negative perception. Another weakness with the available evidence is the general under-representation of older adults within the study populations. Although a varied age range has been evaluated across many studies, the findings cannot clearly be applied to older adults.

The overall safety and efficacy, and place within therapy remains undetermined, but the EAU does recommend duloxetine for SUI or
<table>
<thead>
<tr>
<th>Type of Incontinence</th>
<th>Drug Treatment Class</th>
<th>Specific Agent(s)</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Urge or OAB</td>
<td>Antimuscarinic/anticholinergic agents</td>
<td>Darifenacin, oxybutynin, solifenacin, tolterodine, trospium</td>
<td>Anticholinergic agents are generally first-line therapy. Various forms exist: short-acting, long-acting, and oxybutynin patch and gel. Differences in muscarinic receptor blocking exist. Hypertension, headache, and urinary tract infection are potential adverse effects. Injected via cystoscopy; used in OAB for adults who cannot use or do not respond to antimuscarinic agents.</td>
</tr>
<tr>
<td></td>
<td>β3-adrenergic agonist</td>
<td>Mirabegron</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Neuromuscular blocker</td>
<td>Onabotulinumtoxin A</td>
<td></td>
</tr>
<tr>
<td>Stress incontinence</td>
<td>α-adrenergic agonists</td>
<td>Pseudoephedrine, phenylephrine</td>
<td>Avoid use with hypertension, cardiac arrhythmia. Other side effects include tremor, anxiety, and agitation. Intravaginal estrogen recommended by the European Association of Urology. Improves vaginal and urinary symptoms in SUI, MUI, and UUI. Not FDA approved for SUI; side effects (including nausea, dry mouth, fatigue) may limit its usefulness.</td>
</tr>
<tr>
<td></td>
<td>Local estrogens</td>
<td>Conjugated estrogen, vaginal cream, or estradiol vaginal insert/ing</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Serotonin/norepinephrine reuptake inhibitor</td>
<td>Duloxetine</td>
<td></td>
</tr>
<tr>
<td>Overflow incontinence</td>
<td>α-adrenergic antagonists</td>
<td>Alfuzosin, tamsulosin, silodosin, doxazosin, terazosin</td>
<td>Side effects vary depending on selectivity to receptors in the bladder and/or prostate (alfuzosin, tamsulosin, and silodosin are more specific). For advanced BPH or refractory symptoms. Must weigh risk of urinary retention with improvement in lower urinary tract symptoms.</td>
</tr>
<tr>
<td></td>
<td>5α-reductase inhibitors</td>
<td>Finasteride, dutasteride</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Antimuscarinic agents</td>
<td>Tolterodine</td>
<td></td>
</tr>
<tr>
<td>Functional incontinence</td>
<td>Remove barriers and obstacles, provide schedules or prompted toileting, assistance may be required to transfer on/off commode</td>
<td></td>
<td>Consider therapy to remove any potential cause</td>
</tr>
</tbody>
</table>
| MUI | Focus on symptoms that dominate | | Consider treatments for individual components (i.e., stress and urge) | MUI, mixed urinary incontinence.
mixed UI for temporary improvement when more effective treatments such as surgery are not an option. Doses of 80 mg daily are generally used, and individuals may experience symptom relief as long as they are willing and able to tolerate the side effects. Duloxetine is not recommended for individuals with a CrCl <30 mL/min. It is advised to be used with caution in the elderly within the 2012 American Geriatrics Society Beers Criteria due to the potential for hyponatremia or the increased risk of syndrome of inappropriate antidiuretic hormone.

**Drug Therapy for Overactive Bladder**

Muscarinic antagonists are the most commonly prescribed drugs available for the treatment of UUI. The anticholinergic agents used to treat OAB vary in their pharmacokinetic properties, dosing, and tolerability profiles. There are differences in muscarinic receptor affinities, but efficacy as reported in clinical trials appears to be similar. Oxybutynin is a lipophilic, nonspecific muscarinic antagonist that is available as an immediate-release, extended-release transdermal, or gel formulation. It is effective in reducing UUI symptoms; however, it is associated with high incidence of anticholinergic side effects. Dry mouth, blurred vision, constipation, sedation, and cognitive impairment are all concerns in the older patient. Despite similar efficacy among these formulations, it has been theorized that extended-release transdermal or gel formulations are preferable based on tolerability considerations. For extended-release oral formulations, this is based on the idea that slow release of drug into the bloodstream avoids spikes in serum concentration associated with intermittent doses. For the transdermal formulation, this is based on lower concentrations of the active metabolite N-desethyloxybutynin by avoidance of first-pass metabolism in the liver. The oxybutynin gel formulation also bypasses first-pass metabolism. Data from clinical trials does suggest a reduction in adverse events; however, this was primarily for dry mouth.

Tolterodine is also available in both immediate-release and long-acting formulations and has comparable efficacy to oxybutynin for improvement of OAB symptoms. It is also a nonselective muscarinic antagonist but is less lipophilic than oxybutynin and, therefore, theorized to result in poor distribution into the CNS, resulting in fewer side effects. Comparisons of extended-release tolterodine to either immediate-release or extended-release oxybutynin did show a lower incidence of adverse effects; however, again, this was primarily limited to reduced incidence of dry mouth.

When discussing the use of extended-release or immediate-release preparations, both can be offered as therapy, and there are many factors to consider. In some cases, there may be insurer issues that determine product selection that the prescriber must acknowledge in addition to recognizing improved adherence with once-daily formulations. If immediate-release preparations are unsuccessful or intolerable, then extended-release agents may be considered. If individuals are having sufficient symptom control without side effects, then a change may be unnecessary.

There are two agents that are more selective for the M3 receptor, solifenacin and darifenacin, which are both available in formulations for once-daily dosing. In one study comparing solifenacin to tolterodine, solifenacin significantly improved symptoms of urgency and UI versus tolterodine; however, this study has been criticized because dose escalation was allowed in the solifenacin group but not in the tolterodine group. 

Agents with high M3 selectivity are thought to be associated with relatively higher rates of constipation, but discontinuation rates due to adverse events were not different between the two groups. The potential sparing of M1 receptor-mediated cognitive impairment has only been minimally investigated. Darifenacin’s effect on cognitive function was compared to oxybutynin ER in healthy subjects over the age of 60. Darifenacin-treated subjects scored similar to placebo subjects on delayed recall tests, while subjects receiving oxybutynin ER experienced memory deterioration estimated to be comparable to brain aging of 10 years. This study has limitations such as
short duration, dropouts, differences in baseline characteristics between groups, and questions about dose equivalence.48,49

Trospium is different from other muscarinic antagonists because it is a quaternary ammonium compound and is, therefore, thought to penetrate poorly into the CNS. Trospium is similar in efficacy to oxybutynin IR; dry mouth is reported to occur less often.48 In general, clinicians should not use antimuscarinic agents in individuals with narrow-angle glaucoma unless approved by the treating ophthalmologist, and these agents should also be used very cautiously in the presence of impaired gastric emptying or history of urinary retention. In these situations, benefit versus risk must be carefully considered.37

One recent systematic review evaluated the pharmacological treatment of UI in women, focusing on darifenacin, fesoterodine, oxybutynin, solifenacin, tolterodine, and trospium. The evaluation identified 94 randomized trials of drug efficacy or comparative effectiveness and examined adverse effects and treatment discontinuation secondary to adverse effects. Pharmacological agents were more effective than placebo in improving UI and achieving continence with a low magnitude of benefit. There was a <20% absolute risk difference in continence for all drugs. Pharmacological agents resulted in adverse effects more often than placebo, leading to higher discontinuation rates. None of the agents showed clear superiority compared to one another.50

The FDA approved transdermal oxybutynin from prescription-only dispensing to over the counter (OTC) in 2013. This change involved significant controversy. There were three study types conducted to present information to the FDA to gain approval: a label comprehension study, a self-selection study, and an actual-use study. Based on the results of these studies, the OTC oxybutynin product is only approved to be used by women over 18 years of age for OAB. According to the product label, it should only be used only when symptoms are present for more than 3 months, and individuals should discontinue and speak with a provider if the condition does not improve within 2 weeks.28,51

Now that this product is available OTC without a prescription for women, it is important that patients understand when it is appropriate to use and how to monitor for tolerability and efficacy. It is not approved for men, based on the potential issues of differentiating UI causes from BPH.28 When considering product marketing and packaging, it is clear that this agent is targeting women.

Mirabegron is the first beta-3 adrenergic antagonist approved in the United States. It is a once-daily treatment indicated for OAB in adults with symptoms of UUI, urgency, and urinary frequency.32,52,53 Mirabegron 25- and 50-mg daily doses significantly reduced the number of daily incontinence episodes compared to placebo. The starting dose is 25 mg, and if sufficient response is not seen at 8 weeks it can be increased to 50 mg. Patients with reduced CrCl of 15–29 mL/min or moderate liver disease should not receive more than 25 mg. Increases in blood pressure have been reported, and it is not recommended for use in patients with severe uncontrolled hypertension (systolic and diastolic blood pressure exceeding 180 mmHg or 110 mmHg, respectively). Mirabegron is a moderate CYP2D6 inhibitor and may interact with 2D6 substrates, especially agents with a narrow therapeutic index.29,52,53

Mirabegron appears to demonstrate moderate efficacy in treating OAB. Because there are no anticholinergic properties, this is an advantage, but urinary retention, elevations in blood pressure, and drug interactions may occur. There is limited information regarding long-term safety data.52,53

Another addition to drug therapy involves FDA approval of onabotulinumtoxinA for the treatment of UI in adults due to detrusor overactivity associated with neurological conditions and intolerance or insufficient response to anticholinergic therapy. In 2013, it was also approved for adults in OAB with symptoms of UUI, urgency, and frequency. Upon injection of onabotulinum-
toxinA by cystoscopy—an endoscopic procedure to view the bladder and urethra via a thin, lighted instrument—the bladder relaxes and the storage capacity is increased, reducing episodes of UI. There are many risks associated with this agent, including urinary retention and UTIs.\textsuperscript{28,54,55}

Besides OAB, clinical studies with onabotulinumtoxinA in older adults are limited. In the approval studies for OAB, about 40% of the subjects were over 65, and 15% were 75 or above. UTI and urinary retention were more common in individuals over 65 in both placebo and treatment group. The safety profile was similar for both younger and older subjects.\textsuperscript{28,54}

The recommended dose of onabotulinumtoxinA for OAB is 100 units injected via cystoscope. The needle should be inserted 2 mm into the detrusor, and 20 injections (0.5 mL each) are spaced approximately 1 cm apart. Patients should be observed for at least 30 minutes after the injections and until a spontaneous void has occurred. It is important to note that individuals may be considered for reinjection when the effect of the previous injection has lessened, but not sooner than 12 weeks from the previous bladder injection. The median duration of response based on patient qualification for retreatment was 19–24 weeks when receiving the 100-unit dose according to product labeling.\textsuperscript{54}

In general, no single agent has emerged as the product of choice for treating UUI or OAB.\textsuperscript{48,49} Drug selection is based on the perceived side effect profile, and all patients should be carefully monitored for symptom response and emergence of adverse effects. At this time, there is no clear clinical advantage of the newer versus older agents, and there is a lack of head-to-head clinical trials to determine any one particular agent as superior. Choosing an agent based on uroselective properties has not been demonstrated to be an accurate predictor of successful therapy.\textsuperscript{28} Tolerability, individual preference, or formulary considerations may be the deciding factor in determining the appropriate agent.\textsuperscript{53} Antimuscarinics should begin to work within the first month of initiating therapy, and mirabegron 25 mg is generally effective within 8 weeks. It is important to ensure appropriate follow-up to assess potential adverse effects as well as efficacy.\textsuperscript{28,53}

**Drug Therapy for Overflow Incontinence**

The drug therapy for this type of incontinence will be discussed in the Benign Prostatic Hyperplasia section. Although women can experience this type of incontinence, and there are limited data describing the use of alpha antagonists such as terazosin and doxazosin in these circumstances, the majority of the clinical data in this area have been evaluated in men with urinary symptoms associated with BPH.

**Special Considerations for the Use of Drug Therapy**

There are many factors to consider prior to initiating drug therapy for UI. Comorbid conditions such as dementia, constipation, orthostatic hypotension, history of falling, or other conditions may influence the choice of drug therapy. Other medications that the patient is taking may interact with an agent intended to treat incontinence. For example, adding anticholinergic medications for incontinence to a regimen that includes other anticholinergic medications can result in added side effects. Conversely, the concurrent use of acetylcholinesterase inhibitors with some of the anticholinergic drugs to treat UI may alter the efficacy of each drug and cause undesirable side effects due to a potential state of pharmacological opposition. Acetylcholinesterase inhibitors increase acetylcholine levels in the neural cleft in patients with dementia, and incontinence agents target the muscarinic receptors to decrease acetylcholine. Previous studies demonstrate that bladder anticholinergic agents are associated with cognitive impairment in individuals with dementia, but literature describing concurrent use of acetylcholinesterase inhibitors and anticholinergics is limited to case reports and small observational studies.

In a prospective cohort of nursing home residents, the addition of either tolterodine or oxybutynin to patients already receiving an
acetylcholinesterase inhibitor was evaluated. In individuals with higher levels of baseline functioning, the rate of decline in function (activities of daily living and cognition) was 50% faster when bladder anticholinergics were combined with acetylcholinesterase inhibitors than when acetylcholinesterase inhibitors were used alone. \(^5^6\)

Progression of dementia can exacerbate UI, and this is a challenge for caregivers. Caution should be exercised when anticholinergics are added to a pharmacotherapy regimen in a patient with dementia, as the risk for cognitive and functional decline may not outweigh any improvement in continence. These individuals should be closely monitored when therapy is initiated and on an ongoing basis. \(^2^8\)

It is important to evaluate the safety and efficacy of newer agents in the older adult and elderly population to determine the best choice for pharmacotherapy. Although some of the newer agents may offer better side effect profiles, no clear improvement in efficacy has been demonstrated. Cost is another issue for some older adults, as many of the older agents are available generically, and there may be formulary and insurance restrictions. A sufficient trial should be given, at least 1–2 months, to determine how well any agent is working. Monitor carefully for side effects, objective evidence of incontinence frequency, and patient satisfaction with therapy. If an agent has not produced an adequate response in 2 months, consider discontinuing the drug or switching to another agent in the appropriate category. \(^2^9\)

**Surgery**

Utilizing surgery as an option for the treatment of UI is a consideration when behavioral modifications, pelvic muscle rehabilitation, and/or drug therapy have not been successful. Surgical procedures to treat stress incontinence are intended to correct urethral closure deficiencies and to improve urethrovaginal junction support. Examples in women include bladder neck needle suspension, anterior vaginal repair, or suburethral sling procedures. There are potential adverse outcomes and risks with surgery, including urge incontinence, voiding difficulties, or pelvic organ prolapse. \(^3^9\) In men, surgical options for SUI include collagen or an artificial urinary sphincter. \(^3^2\)

For patients with overflow incontinence, there are not any effective surgical options for bladder underactivity. After reversible causes are excluded, self-catheterization by the patient or a caregiver several times a day is one effective management strategy to empty the bladder. Urethral overactivity is typically caused by some type of anatomic obstruction. In men, this is often explained by benign prostatic enlargement. \(^3^2\)

**Benign Prostatic Hyperplasia**

BPH is a common condition affecting older men and a cause for significant urinary symptoms that alter a man's quality of life. Age is the predominant factor in establishing the prevalence and histopathologic significance of BPH. Prostatic hypertrophy develops typically after age 40, with a 50% prevalence by age 60 and a prevalence approaching 90% by age 85. Autopsy studies show that an estimated 80% of elderly men have microscopic changes consistent with BPH. Approximately half the individuals with these changes experience moderate to severe lower urinary tract symptoms. \(^5^7-5^9\)

The prostate gland is surrounded by a dense fibrous capsule composed of smooth muscle cells, glandular cells, and supportive stromal cells. \(^6^0\) Alpha reductase is also found within the prostate and facilitates the conversion of testosterone to dihydrotestosterone (DHT). At birth, prostate size resembles that of a pea, growing during puberty to reach an adult size by ages 25–30. A second growth spurt occurs around age 40, and growth continues through the seventh or eighth decades. The exact etiology of BPH is unknown; however, age-related hormonal changes, type II 5-alpha reductase, and circulating androgens such as DHT are involved. The pathogenesis of BPH is due to static factors, including glandular enlargement of the prostate, as well as to dynamic factors such as excessive alpha-adrenergic tone of the stromal compo-
nent of the prostate gland, bladder neck, and posterior urethra. This leads to the narrowing of the urethral lumen by contraction of the prostate gland surrounding the urethra. Ultimately, anatomic enlargement of the prostate gland and narrowing of the urethral lumen results in obstructed urinary outflow.57,60

Individuals with BPH often experience a wide range of signs and symptoms of disease that are classified as obstructive or irritative. Obstructive symptoms, known as bladder outlet obstruction (BOO) or prostatism, result from decreased bladder emptying and include hesitancy, urinary stream weakness, intermittency, and the sensation of incomplete bladder emptying. Irritative symptoms, which occur in 50% to 80% of patients with BPH, typically occur later in the disease process and can be attributed to long-standing bladder neck obstruction. These symptoms often result in frequency, nocturia, and urgency. Symptoms of BPH are highly variable and may improve, worsen, or remain stable; it is not necessarily a progressive condition in all men.57,60 An individual’s ability to tolerate symptoms is often the motivation to seek treatment.

Men with troubling lower urinary tract symptoms (LUTS) should be evaluated to assess severity and the potential for causes other than BPH, such as prostatitis and bladder or prostate cancer. It is important to establish that symptoms are truly due to BPH and not to other diagnoses of LUTS.59,60 The American Urological Association Symptom Index (AUA-SI) for BPH and the Disease-Specific Quality of Life Question is a validated tool that can be used to objectively determine BPH severity in men seeking treatment (see Figure 9-2) and is superior to an unstructured interview in quantifying the severity and frequency of symptoms.59 Refer to Figure 9-3 for an algorithm for diagnosis and treatment from the American Urological Association.59

Most recent guidelines from the American Urological Association include two algorithms for approaching the evaluation and treatment of LUTS (see Figures 9-3 and 9-4). The first describes basic management and classifies diagnostic tests as either recommended (should be performed on every patient during the initial evaluation) or optional (test of proven value in the evaluation of select patients). Optional tests are generally performed during a detailed evaluation by a urologist. If the initial evaluation reveals LUTS associated with results of a digital rectal exam suggesting prostate cancer, hematuria, abnormal prostate-specific antigen levels, recurrent UTI, palpable bladder, history/risk of urethral stricture, and/or a neurological disease raising the likelihood of a primary bladder disorder, patients should be referred to a urologist for follow-up before initiation of treatment.

If initial evaluation finds the presence of LUTS only, with or without mild prostate enlargement, treatment is not warranted, and the patient can be seen again when symptoms become bothersome. However, if the LUTS are bothersome to the patient, there may be several causes, including benign prostatic obstruction, OAB, and nocturnal polyuria. If nocturnal polyuria is the predominant symptom, and the patient awakens two or more times nightly to void, guidelines recommend that a frequency volume chart be completed by the patient. Nocturnal polyuria is diagnosed when >33% of the 24-hour total urine output occurs at night. On diagnosis, fluid intake should be reduced and pharmacologic agents (i.e., desmopressin) may be considered. When symptoms persist, the patient should be treated as having no significant nocturia, and medical and pharmacological treatments should be employed as necessary. Initial interventions of modifiable factors should include decreased nocturnal fluid intake, increased activity, and avoidance of excess alcohol and other irritating foods.

Basic management of patients with bothersome LUTS includes alteration of modifiable factors and lifestyle advice, such as increasing activity. Modifiable factors include concomitant drugs, excess fluid intake at night, excess alcohol intake, and highly seasoned or irritating foods.61
### AUA-BPH Symptom Score

<table>
<thead>
<tr>
<th></th>
<th>Not at all</th>
<th>Less than 1 time in 5</th>
<th>Less than half the time</th>
<th>About half the time</th>
<th>More than half the time</th>
<th>Almost always</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Over the past month, how often have you had a sensation of not emptying your bladder completely after you finished urinating?</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>2. Over the past month, how often have you had to urinate again less than 2 hours after you finished urinating?</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>3. Over the past month, how often have you found you stopped and started again several times when you urinated?</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>4. Over the past month, how often have you found it difficult to postpone urination?</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>5. Over the past month, how often have you had a weak urinary stream?</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>6. Over the past month, how often have you had to push or strain to begin urination?</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>7. Over the past month, how many times did you most typically get up to urinate from the time you went to bed at night until the time you got up in the morning?</td>
<td>None</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5 or more times</td>
</tr>
</tbody>
</table>

**Total Symptom Score**

<table>
<thead>
<tr>
<th>None</th>
<th>1 time</th>
<th>2 times</th>
<th>3 times</th>
<th>4 times</th>
<th>5 or more times</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
</tbody>
</table>

### The Disease-Specific Quality of Life Question

The International Prostate Symptom Score uses the same seven questions as the AUA Symptom Index (presented above), with the addition of the following Disease-Specific Quality of Life Question (bother score), scored on a scale from 0 to 6 points (delighted to terrible):

“If you were to spend the rest of your life with your urinary condition just the way it is now, how would you feel about that?”

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*Figure 9-2. The American Urological Association Symptom Index for benign prostatic hyperplasia and the Disease-Specific Quality of Life Question.*

Figure 9-3. Basic management of lower urinary tract symptoms (LUTS) in men.

AUA-SI, American Urological Association Symptom Index; DRE, digital rectal exam; PSA, prostate-specific antigen.

**Figure 9-4.** Detailed management for persistent bothersome LUTS after basic management.

Many pharmacological agents must be avoided in men with BPH, because of the potential to worsen symptoms. Alpha-adrenergic agonists used as decongestants (oral or intranasal) can lead to muscle contraction secondary to alpha-adrenergic receptor stimulation in the prostate. Bladder emptying may be affected because of changes to the urethral lumen. Examples include pseudoephedrine, ephedrine, or phenylephrine. In general, drugs with anticholinergic properties have the potential to decrease contractility of the urinary bladder detrusor muscle. This is especially problematic in patients with BPH with a narrowed urethral lumen and an enlarged prostate gland. This loss of effective detrusor contraction can result in urinary retention. Example agents include antihistamines, tricyclic antidepressants, antipsychotics, or muscle relaxants. Despite this, anticholinergic drugs must be used carefully when LUTS persist despite traditional interventions.

In addition, opiates may impair autonomic function, and diuretics may lead to polyuria. Theoretically, testosterone replacement regimens used in primary or secondary hypogonadism should be used cautiously, as these agents can be metabolized by the prostate to DHT. If symptoms persist despite all of the above, pharmacologic therapy can be considered, and follow-up assessment is recommended to assess response to therapy. Time to follow-up is variable depending on the agent chosen. Successful treatment can be re-evaluated annually.

Treatment of BPH

Traditionally, the primary treatment goal has been to alleviate bothersome LUTS. More recently, treatment has addressed the prevention of disease progression. However, because BPH is a disease characterized by symptoms, treatment continues to be focused on determining the severity of the symptoms and the individual’s desire to relieve those symptoms. Generally, pharmacologic therapy focuses on reducing the dynamic factor via agents that relax prostatic smooth muscle, reducing the static factor via agents that interfere with testosterone’s stimulatory effect on prostate gland enlargement, or a combination of both. Treatment and management options include watchful waiting, drug therapy, and surgical interventions. The American Urology Association Guidelines on the Management of BPH are a primary tool governing treatment decisions in the United States. Within this guideline, the AUA-SI and Quality of Life questionnaire shown in Figure 9-2 is used to survey patients to identify their total symptom score. Disease severity is classified as mild, moderate, or severe based on the score (mild is ≤7, moderate is 8–19, and severe is ≥20). According to the guidelines, patients with either mild symptoms or those with moderate-severe scores who are not bothered by their LUTS should be managed using watchful waiting. Generally, these individuals will not benefit from therapy because symptoms do not have a significant impact on the quality of life. Watchful waiting involves annual visits for reassessment and education about behavioral strategies that may assist with symptom management (i.e., avoiding medications that can exacerbate BPH).

Individuals with bothersome moderate to severe symptoms and a score ≥8 have several treatment options available, including medical watchful waiting, medical therapies (alpha-adrenergic blockers/antagonists or 5-alpha reductase inhibitors [5ARIs]), minimally invasive therapies (transurethral microwave heat treatments or transurethral needle ablation), or surgical therapies (transurethral resection of the prostate or open prostatectomy). The risks and benefits of each option should be discussed with the patient to allow the most individualized therapy. If a patient’s LUTS are bothersome despite basic management strategies, a urologist should be consulted. If drug therapy is considered, agents should be chosen based on coexisting OAB symptoms and prostate size/prostate-specific antigen (PSA) levels (see Figure 9-4).

Coexisting OAB symptoms and prostate size (or serum PSA levels) can help to determine what kind of drug therapy is most appropriate. When a patient has BOO in addition to OAB symptoms, a combination of alpha-adren-
ergic blockade and anticholinergic therapy is warranted. However, when BOO symptoms are more significant, alpha-adrenergic blockers (AABs) are the first line. When the prostate is enlarged, alpha blockers alone, 5ARIs alone, and/or a combination of the two have shown to be most efficacious.59

Current drug treatment options for BPH generally include AABs (also known as alpha-adrenergic antagonists), 5-alpha reductase inhibitors (5ARIs), or a combination of the two classes. Ideally, drug therapy should be initiated with a single agent before combination. Generally, AABs are the preferred first agent because they have a faster onset and are more effective than 5ARIs. AABs are also effective in reducing LUTS independent of prostate size, have no effect on PSA, and are associated with less sexual side effects compared to 5ARIs. However, if a patient has a significantly enlarged prostate (>40 g) and cannot tolerate the cardiovascular effects of AABs, 5ARIs are recommended. For patients at high risk of developing complications associated with BPH (prostate gland >40 g and PSA ≥1.4 ng/mL), combination therapy with both AABs and 5ARIs is appropriate.62,63 In these patients, combination therapy quickly relieves symptoms, delays disease progression, and reduces the need for surgical intervention.57

Short-term improvements, including the relief of BPH symptoms and an increased urinary flow, have been demonstrated with both AABs and 5ARI therapy. No clear evidence is available to prove that AABs alone can reduce the need for future prostate surgical procedures, but 5ARIs have shown reductions in the need for surgical interventions.66 Overall, drug therapy is not as efficacious as surgical interventions; however, this option may offer symptomatic relief, with fewer and less severe associated adverse events.59

AABs relieve symptoms in men suffering from moderate to severe BPH. Smooth muscles in the prostate gland contract in response to stimulation by alpha receptors, leading to constriction of the prostatic urethra. AABs improve LUTS by encouraging smooth muscle relaxation. AABs used in the treatment of BPH include alfuzosin, doxazosin, tamsulosin, terazosin, and silodosin. With the emergence of newer, more convenient, and safer options, older AABs such as phenoxybenzamine and prazosin are not currently recommended in the treatment of BPH.59 Tamsulosin and silodosin are third-generation AABs, and the remaining are second-generation. In addition to prostate effects, doxazosin and terazosin, considered to be nonselective alpha, adrenergic antagonists, also decrease blood pressure by their effect on vascular smooth muscle and carry an FDA labeling for hypertension. However, AABs are not preferred as single-drug therapy for treatment of both BPH and hypertension in a patient.57 Due to their mechanism of action and peak onset, immediate-release formulations of doxazosin and terazosin should be administered at bedtime.57

Tamsulosin, alfuzosin, and silodosin are newer agents that treat constriction of prostate smooth muscle.59,64,69 Tamsulosin is a selective antagonist of alpha1a adrenoreceptors of the prostate, whereas alfuzosin and silodosin are selective antagonists of postsynaptic alpha, adrenoreceptors located in the prostate, bladder base, bladder neck, prostatic capsule, and prostatic urethra.67,68 Alpha blockers may cause orthostatic hypotension, and nonselective agents must be started at a low dose and titrated to efficacy; dose titration is not required for alfuzosin.68 By targeting the lower urinary tract and prostatic smooth muscles, tamsulosin and alfuzosin appear to have favorable safety profiles; however, warnings for syncope and orthostatic hypotension remain in the product labeling.66,67 The incidence of orthostatic hypotension is increased when alpha blockers are combined with drugs that can exacerbate hypotension, and caution must be exercised in these situations.58

Alfuzosin, doxazosin, tamsulosin, and terazosin are recommended as appropriate treatment options for LUTS secondary to BPH, and, according to the most recent AUA Guideline, all are equally efficacious in the management of LUTS secondary to BPH.59 There are differ-
ences among these drugs regarding adverse event profiles, but in terms of clinical effectiveness the drugs are similar. Treated patients can expect a 30% to 40% improvement in AUA-SI within 2–6 weeks, depending on the need for up-dose titration.\textsuperscript{57} Time to peak effect for BPH symptoms differs among the agents: tamsulosin and alfuzosin generally will peak within several days, whereas doxazosin and terazosin may take several weeks.\textsuperscript{57} Methodically sound trials that compare these agents against each other are needed to show superiority for any particular one.\textsuperscript{59} Numerous trials document that doxazosin, terazosin, alfuzosin, and tamsulosin are effective as single agents in both symptom relief and increased urine flow when compared to placebo. Doxazosin monotherapy has also demonstrated decreased long-term complications of BPH, including UI, urinary retention, and renal insufficiency.\textsuperscript{57} Unlike tamsulosin, silodosin, the most recently approved AAB, requires dosage adjustment for renal impairment (50% of normal dosing for CrCl <50 mL/min, contraindicated in CrCl <30 mL/min) and hepatic impairment (contraindicated with Child-Pugh \textgreater 10), has increased potential for drug interactions, and limited experience in clinical practice. Due to these factors, tamsulosin is currently the preferred third-generation AAB.\textsuperscript{79} DHT is an androgenic hormone that stimulates growth of the prostate. The 5ARIs, finasteride and dutasteride, inhibit the conversion of testosterone to DHT.\textsuperscript{58} These medications offer more benefit when the prostate volume is \textgreater 40 mL.\textsuperscript{65} One meta-analysis suggested that finasteride is more effective in men with large versus small prostate size.\textsuperscript{69}

Alpha reductase inhibitors are appropriate and effective options for individuals with prostate enlargement and LUTS and have been shown to modify the clinical disease course and potentially reduce the risk of urinary retention and surgical interventions.\textsuperscript{59,70} PSA levels are decreased with 5ARI therapy, so it is recommended to obtain baseline PSA levels prior to beginning treatment. Although the guidelines suggest that cancer detection is not masked, it is recommended to perform PSA and rectal exams annually, and any increases in PSA should be evaluated for medication noncompliance and/or prostate cancer.\textsuperscript{57,59}

Differences exist between finasteride and dutasteride. Finasteride competitively inhibits type II 5-alpha reductase and lowers intraprostatic DHT by 80% to 90% and serum DHT by 70%. On the other hand, dutasteride is a dual nonselective inhibitor of type I and II 5-alpha reductase. Intraprostatic DHT production is quickly and completely suppressed, and serum DHT is decreased by about 90% with dutasteride. Despite these pharmacodynamic differences, direct comparison trials have not shown any advantage of these actions in favor of dutasteride, and both agents have demonstrated comparable efficacy in reducing prostate size.\textsuperscript{57}

One important consideration is that 5ARIs are not as effective as an alpha blocker in improving LUTS. These agents are not an appropriate treatment recommendation for men without prostate enlargement.\textsuperscript{59} Alpha-reductase inhibitors do not provide immediate symptom relief; 6 months of therapy is generally required to achieve clinical benefit.\textsuperscript{71} Overall, an evidence-based review determined that 5ARI therapy partially relieves symptoms but is less effective for symptom control than alpha blocker therapy. However, due to the more progressive disease in men with larger prostate glands or for those with higher PSA values, 5ARIs have a role in modifying BPH and its clinical course that is not found with alpha blockers.\textsuperscript{59,72}

There are instances when combination therapy with alpha blockers and 5ARIs may be beneficial, especially in men with larger prostate size and elevated PSA.\textsuperscript{59,62,73} These patients appear to be at increased risk for disease progression, highlighted by worsening symptoms and complications of disease.\textsuperscript{57} Combination therapy makes sense theoretically in that the alpha blocker will begin to work for symptomatic relief until the finasteride can begin to reduce prostate size. Combination therapy with finasteride and doxazosin has been most investigated.\textsuperscript{59} Recent studies have been conducted involving
dutasteride and tamsulosin, and this prompted FDA approval for dutasteride and tamsulosin in combination for the treatment of symptomatic BPH in men with an enlarged prostate.\textsuperscript{73,74} Two large studies, the MTOPS and the ComBAT, evaluated combination drug therapy versus monotherapy using either doxazosin and finasteride or dutasteride and tamsulosin. Although there were baseline differences between the MTOPS and ComBAT study groups, the results of the two studies support the use of combination therapy in men with prostate enlargement and moderate to severe LUTS in achieving further symptomatic benefit.\textsuperscript{74-77}

Alpha blockers, 5\textsuperscript{ARIs}, or even surgery (discussed below) may all improve bladder emptying or urinary flow. However, there is a potential role for the addition of an anticholinergic agent such as oxybutynin or tolterodine to improve irritative voiding symptoms (e.g., frequency and urgency associated with BPH).\textsuperscript{57} LUTS, BPH, and OAB are related, but the mechanisms linking them are not well understood. One theory is that BOO may lead to OAB.\textsuperscript{78} Anticholinergic agents can reduce detrusor contractions by blocking muscarinic receptors in the detrusor muscle. Because older adults are especially sensitive to the CNS adverse effects and dry mouth of anticholinergic drugs, they must be chosen carefully and used with extreme caution, as discussed in the Types of Urinary Incontinence section of this chapter. The current AUA Clinical Practice Guideline suggests that the use of anticholinergic agents in combination with AABs is appropriate in patients with mixed OAB and BOO.\textsuperscript{70} Use of anticholinergic agents in individuals with BPH may also lead to acute urinary retention or increased postvoid residual (PVR) urine volume.\textsuperscript{57,78} Therefore, baseline PVR is recommended before initiation of anticholinergic therapy.\textsuperscript{70}

**Emerging Therapies**

Phosphodiesterase (PDE) inhibitors increase the concentration and prolong the activity of intracellular cGMP, hereby reducing smooth muscle tone of the detrusor, prostate, and urethra. Until now, 11 different PDEs have been identified, of which PDE 4 and PDE 5 are predominant in the transition zone of the human prostate, bladder, and urethra.\textsuperscript{80,81} Nitric oxide might also be involved in the micturition cycle by inhibiting reflex pathways in the spinal cord and neurotransmission in the urethra, prostate, or bladder.\textsuperscript{82} Sildenafil, tadalafil, and vardenafil have been studied in recent trials both alone and with AABs. These trials demonstrated that all PDE 5 inhibitors (PDE5Is) significantly and consistently reduced International Prostate Symptom Scores by approximately 17\% to 35\%. Both bladder storage and voiding symptoms decreased equally during treatment with PDE5Is.\textsuperscript{83-90} However, trials were conducted on a limited number of patients for a very short duration (maximum 12 weeks) and, therefore, PDE5Is are not currently recommended for use in LUTS.\textsuperscript{91} Although tadalafil gained FDA approval for BPH, current guidelines do not recommend it as first-line therapy.\textsuperscript{59,91}

**Dietary Supplements**

In addition to pharmacological agents, alternative therapies may be considered by some patients. Saw palmetto plant extract (Serenoa repens) has been used to manage the LUTS of BPH. The mechanism of action of saw palmetto is unknown in the management of BPH. Possible proposed mechanisms include preventing the conversion of testosterone to DHT, potential anti-inflammatory activity, or prostate epithelial involution similar to effects noted with other 5\textsuperscript{ARIs}.\textsuperscript{91} This proposed mechanism of saw palmetto suggests a possible drug interaction between this product and standard drug therapy for BPH. Individuals should be counseled and warned about this combination. There have been mixed opinions regarding the value of saw palmetto. Although trials and meta-analyses exist that clearly demonstrate the efficacy of Serenoa repens in improving symptom scores and maximum flow rate, current practice guidelines do not recommend saw palmetto or other forms of phytotherapy for BPH, because of the lack of long-term studies.\textsuperscript{59,92-95}
Surgery

Surgery is another intervention in the management of BPH. In situations where medical treatment is ineffective, in patients with moderate to severe symptoms, or for individuals who prefer it, surgery is an option. Surgery is more effective for men with moderate symptoms of BPH or in men with enlarged prostates <50 g compared to watchful waiting in improving genitourinary symptoms and reducing treatment failure. Compli-
cations reported include sexual dysfunction, irritation with voiding, bladder neck contracture, need for blood transfusions, infection, and hematuria. Newer surgical procedures include transurethral needle ablation, transurethral incision of the prostate, and transurethral microwave therapy. These procedures are minimally invasive, short, and an option for men who are poor surgical candidates for TURP.

Men experiencing complications from BPH, such as acute urinary retention, also may opt for surgical intervention as an initial therapy, depending on individual risks versus benefits. Surgical removal of the prostate, or prostatectomy, provides the highest rate of symptom improvement, but it also carries the greatest complication risk. Transurethral resection of the prostate (TURP) is considered the standard surgical therapy for BPH because of the extensive success and follow-up data that are published with this procedure. Some newer surgical techniques are available, but the TURP remains the preferred technique.

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Complications reported include sexual dysfunction, irritation with voiding, bladder neck contracture, need for blood transfusions, infection, and hematuria. Newer surgical procedures include transurethral needle ablation, transurethral incision of the prostate, and transurethral microwave therapy. These procedures are minimally invasive, short, and an option for men who are poor surgical candidates for TURP.
Case 1: Incontinence in a Nursing Home Resident with Dementia

Setting:
Quarterly care conference.

Subjective:
JD is an 85-year-old Caucasian male resident of a long-term care facility. He has no complaints, but the nursing staff is concerned about an increased frequency of UI episodes.

Past Medical History:
JD was admitted to the long-term care facility for care on the Alzheimer Disease and Related Dementia unit, with a mini-mental exam score of 15/30, a decline of 2 points from 1 year ago. His past medical history is significant for hypertension and BPH.

Medications:
Donepezil 10 mg once daily, hydrochlorothiazide 25 mg once daily, lisinopril 20 mg daily, multivitamin daily, docusate 100 mg two times/day, bisacodyl 10 mg once daily as needed for constipation, tylenol PM one tablet at bedtime.

Allergies:
NKDA.

Social History:
Unknown.

Family History:
Noncontributory.

Objective:
Ht 5’10˝, Wt 72 kg, BP 90/65 mmHg, P 75 BPM, RR 18, and T 37°C.

Physical Examination:
Unremarkable; assessment of his functional abilities shows limitations in his activities of daily living, requiring assistance with bathing and dressing.

Labs:
Normal CBC, sodium 129 mEq/L, potassium 3.4 mEq/L, chloride 100 mEq/L, carbon dioxide 29 mEq/L, fasting glucose 85 mg/dL, creatinine 1.2 mg/dL, and blood urea nitrogen 28 mg/dL. (Calculated CrCl = 46 mL/min.)

Assessment:
1. Urinary symptoms due to untreated BPH exacerbated by unnecessary anticholinergic medication, diuretic, and cholinesterase inhibitor.
2. Blood pressure and electrolytes such as sodium and potassium are either low or approaching the low end of the desired range, possibly associated with the thiazide diuretic.
3. Alzheimer disease: Cognitive symptoms show a slight decline over the previous year and may be exacerbated by the anticholinergic medication. A drug interaction between donepezil and the anticholinergic is a concern. Complaints of insomnia are presumably a reason the Tylenol PM was started; however, this is not formally documented and is not presenting as a current complaint.
Plan:
1. Discontinue the Tylenol PM related to urinary retention symptoms. If urinary symptoms persist, recommend initiation of tamsulosin 0.4 mg daily. Obtain urine sample to rule out possible UTI as a cause of symptoms. Monitor blood pressure with addition of alpha blocker. Monitor cognition with removal of anticholinergic medication.
2. Continue lisinopril and decrease the dose of hydrochlorothiazide to 12.5 mg daily. Monitor blood pressure and serum electrolytes.
3. Discontinue Tylenol PM (above) and continue donepezil therapy at this time while observing changes in urinary symptoms and cognition. Monitor sleep patterns and level of alertness.

Rationale:
1. It is possible that urinary symptoms may resolve simply with elimination of the anticholinergic medication. If not, alpha blockers are considered first-line treatment for BPH symptoms, but nonselective agents such as doxazosin or terazosin may exacerbate JD’s low blood pressure. This is less of a concern with tamsulosin but can still be problematic, so careful monitoring of blood pressure is required during drug initiation. Reduction in the thiazide diuretic dose may offset some of the hypotensive effect of tamsulosin.
2. JD is receiving appropriate medications for an individual with hypertension and CKD; however, his blood pressure is low and he is experiencing a mild amount of hyponatremia and hypokalemia. It is not clear the extent to which the diuretic may be exacerbating incontinence symptoms, but this can be re-evaluated as therapy for BPH if initiated.
3. It is difficult to evaluate JD’s true magnitude or quality of response to a cholinesterase inhibitor while there is an antagonizing medication taken concomitantly. Therefore, no changes to the donepezil should be made until this complicating factor is removed. It is also unclear whether the cholinesterase inhibitor is worsening urinary symptoms, but due to JD’s stable cognitive status changes to donepezil should be avoided. After the effects of the tamsulosin and diuretic reduction have been observed, possible interactions between the cholinesterase inhibitor and urinary symptoms can be evaluated. It is difficult to discern whether the lack of a documented indication for the Tylenol PM is simply oversight or if the drug can be accurately assessed as unnecessary. In light of his urinary symptoms and dementia with cholinesterase inhibitor use, it is more prudent to discontinue Tylenol PM at this time, while monitoring for any possible re-emergence of insomnia symptoms.

Case Summary:
JD is typical of an older man with multiple coexisting medical conditions and pharmacotherapeutic treatments. The chief complaint involves urinary symptoms; however, it is evident that the current medication regimen and any changes made to it carries implications for his other comorbid conditions. Drug therapy interventions must be made in a careful stepwise approach considering the potential impact on the target disease state and comorbid disease states. In this case, discontinuation of Tylenol PM and reduction of hydrochlorothiazide are the only two interventions taken initially, followed by possible initiation of tamsulosin if urinary symptoms persist. At the same time, the hope is to maximize the effectiveness of donepezil and defer making any changes to donepezil unless absolutely necessary. The two initial changes may not only impact the chief complaint but also the blood pressure, electrolytes, and cognition.
**CASE 2: A COMMUNITY-DWELLING WOMAN WITH HYPONATREMIA**

**Setting:**
Outpatient/assisted living setting.

**Subjective:**
MM is a 92-year-old Caucasian woman who resides in an assisted living facility. She is being evaluated today in the emergency department of her local hospital. Although there are no known baseline deficits in cognition and she is usually continent, she has developed new onset of confusion and falls. Staff report she was found on the floor of her room and complained of hitting her head.

**Past Medical History:**
MM has a history of glaucoma, hypertension, osteoarthritis, and osteopenia. She had an appendectomy in 1976 and was treated for a UTI 3 weeks ago.

**Medications:**
Timolol 0.25% solution, instill 1 drop in both eyes twice daily, acetaminophen 500 mg four times daily, calcium carbonate 500 mg three times daily, vitamin D 800 IU daily, lisinopril 10 mg daily, hydrochlorothiazide 25 mg daily, omeprazole 20 mg daily.

She recently completed a course of antibiotics for the UTI. She receives medication reminders from facility staff, who confirm that she took all of her antibiotic and regularly-prescribed medications.

**Allergies:**
Penicillin.

**Social History:**
Retired music teacher, widowed 9 years ago. Two adult children in good health.

**Objective:**
Ht 5’2˝, Wt 48 kg, BP 114/65 mmHg, P 85 BPM, RR 18, T 38°C

**Physical Examination:**
Thin, confused elderly female in mild distress; otherwise, physical findings are unremarkable.

**Labs:**
UA reveals cloudy urine, negative for nitrite and leukocyte esterase, with no bacteria or WBC. CBC reveals WBC 7.2, hemoglobin 12.1, hematocrit 36%, platelets 202.

**Chemistry Panel:**
Sodium 123 mEq/L, potassium 4.0 mEq/L, chloride 110 mEq/L, and carbon dioxide 28 mEq/L, glucose 92 mg/dL, creatinine 1.0 mg/dL, and blood urea nitrogen 38 mg/dL. Calcium 9.2 mg/dL, phosphorus 2.9 mg/dL, and magnesium 1.5 mg/dL. (Calculated CrCl = 26 mL/min.)

**Assessment:**
1. Falls
2. Hyponatremia
3. Hypomagnesemia and need for medication management
Plan
1. Perform a complete falls assessment. This includes imaging of her brain to rule out head trauma.
2. Discontinue hydrochlorothiazide.
3. Discontinue omeprazole 20 mg daily.

Rationale:
1. MM should receive imaging of her brain to rule out head trauma, such as a subdural hematoma. Her assisted living environment should be assessed for clutter, loose carpets, and other fall hazards. In addition, her serum electrolyte abnormalities should be addressed to further decrease her risk factors for falls (see rationales below). Physical therapy can be recommended to restore any loss of ambulation ability from the recent fall.
2. MM is an elderly woman with hyponatremia that is likely due to hydrochlorothiazide. Even mild hyponatremia increases the risk of falls and may also be responsible for the change in mental state and confusion. Also, based on her present creatinine clearance calculation, MM doesn’t meet the minimal renal function parameters for successful hydrochlorothiazide use. Addition of salt tablets to the regimen would not correct the underlying cause. Discontinuation of the diuretic is best in this case because the cause is more linked to a water deficit and not to a deficiency of salt.
3. MM does not have a diagnosis that justifies use of omeprazole and has mild hypomagnesemia, which could be an adverse effect of omeprazole. Symptoms of the low magnesium, such as muscle cramps and nausea, do not seem to be present. Therefore, discontinuation of the proton pump inhibitor is recommended. Serum magnesium should be monitored after discontinuation of omeprazole and supplementation with magnesium citrate can occur if the magnesium serum concentration does not return to normal (1.8–3.0 mg/dL).

Case Summary:
MM illustrates a common situation, in which a frail elderly woman develops electrolyte disturbances and falls that might be due to her medication regimen. Thiazide diuretics are not recommended in patients with very low creatinine clearance and are a frequent cause of hyponatremia among elderly patients. In addition, MM is receiving omeprazole without a documented need or diagnosis. Chronic use of omeprazole in the elderly with impaired renal function may lead to low magnesium levels. The best approach to this problem is to discontinue the omeprazole.
CHAPTER SUMMARY

Renal function declines with age, and older patients will frequently develop CKD as they enter their 80s and 90s. Also, the elderly often have other comorbid diseases, such as diabetes and hypertension, which may lead to further deterioration in their renal function. This decline in renal function, in addition to diuretic use and changes in cognition and environment, increase the risk of dehydration and imbalances in serum sodium. To estimate renal function, pharmacists must calculate the patient’s creatinine clearance and assess the older patient’s medication regimen to be sure that appropriate renal protection therapies are being utilized and that drugs are screened for their potential to accumulate.

The prevalence of UI increases with age, although it is not considered an expected part of aging. Age-related physiologic changes must be taken into consideration when diagnosing and classifying the various forms of UI. Behavioral rehabilitation techniques, medications, and surgery are all possible treatments but must be chosen only after reviewing the goals of therapy with the individual patient. BPH is the most common urologic condition of aging men. A wide range of signs and symptoms occur in BPH, and it is the individual’s ability to tolerate the symptoms that is usually the motivating factor in seeking treatment. Alpha blockers and/or 5ARIs are the drugs utilized most, as well as surgical intervention. Information from future long-term studies will help define the role of medication therapy for both symptom improvement and to delay disease progression of BPH.

SELF-ASSESSMENT QUESTIONS

1. What are the common changes in physiology of the kidney that occur with age, and how do these changes impact the development of CKD?

2. What are the advantages and disadvantages in older persons of the commonly used equations to calculate creatinine clearance?

3. Explain what common electrolyte disorder might occur in an older person on a thiazide diuretic. What is the mechanism for this effect?
4. What are the major differences between the signs and symptoms of the types of UI? Explain how these symptom differences can help differentiate the types of UI in a patient.

5. Under what circumstances would an alpha blocker cause UI? Under what circumstances would an alpha blocker be helpful in treating UI?

6. In a patient with OAB, how do you choose between the different anticholinergic medications approved to treat this disorder?

7. In an older man with BPH involving severe LUTS, what is a recommended treatment?

8. In a man with BPH, under what circumstances is it most justified to use the combination of an alpha blocker and an alpha-reductase inhibitor?

References


Learning Objectives

1. Identify the prevalence and clinical presentation of endocrine disorders, including diabetes mellitus, obesity, thyroid disorders, and sexual dysfunction, among older adults.

2. Evaluate the management of older adults with endocrine disorders compared to younger patients.

3. Assess the potential effects of major endocrine disorders on common comorbid diseases in older adults and on quality-of-life issues.

4. Critique major studies of diabetes mellitus that enrolled older adults regarding the studies’ application to clinical practice.

5. Develop a treatment plan appropriate for older adults with selected endocrine disorders.

Key Terms and Definitions

Graves’ Disease: An immune system disorder characterized by painful, red eyes due to inflammation. Eyelids and tissues around the eyes are swollen with the eyeballs bulging out of their sockets.

Hemoglobin A1c (HbA1c): A minor component of hemoglobin to which glucose is bound. HbA1c is also referred to as glycated hemoglobin; it provides a measure of glucose control over the past 3 months.

Hormone Therapy (HT): A term, along with menopausal hormone therapy, that describes the hormones used to treat menopausal symptoms. In the past, this therapy was called hormone replacement therapy. The newer term reflects the fact that the estrogen and progestin concentrations are not returned to premenopausal levels.

Macrovascular Complications: Diseases of the larger blood vessels resulting in atherosclerotic vascular disease.
MICROALBUMINURIA: Urinary albumin excretion between 30 and 300 mg in a 24-hour period.

MICROVASCULAR COMPLICATIONS: Diseases of the small blood vessels that may lead to loss of sensation and foot ulcers.

SECRETAGOGUES: A substance or hormone that causes or stimulates secretion.

T3 (TRIIDOTHYRONINE): An iodine-rich thyroid hormone formed from one molecule of monoiodotyrosine and one of diiodotyrosine. Most of the circulating T3 is the result of the enzymatic degradation of T4 in extrathyroidal peripheral tissues. T3 is extensively bound to albumin, thyroxine-binding globulin, and transthyretin.

T4 (THYROXINE): An iodine-rich thyroid hormone formed from two molecules of diiodotyrosine in the thyroid gland. T4 is extensively bound to albumin, thyroxine-binding globulin, and transthyretin.

THYROIDITIS: An inflammation of the thyroid gland in which there is a release of thyroid hormone that results in a temporary hyperthyroid state.

THYROID-STIMULATING HORMONE (TSH): A hormone secreted by the pituitary gland; stimulates thyrotropin receptors to regulate the activity of the thyroid gland.

Introduction

The endocrine system affects almost every organ in the body physiologically. It regulates glucose and thyroid metabolism, maintains muscle and skeletal mass and normal gonadal functioning, and has many other roles. Similar to other systems, the endocrine system may undergo diverse changes due to aging. The best recognized age-related endocrine change occurs within the hypothalamic-pituitary-adrenal axis with the onset of menopause in middle-aged women. The secretion of growth hormone and the serum concentration of insulin-like growth factor may decrease with age. The secretion of dehydroepiandrosterone from the adrenal cortex may also decline with advancing age, and older adults may have greater variability in serum cortisol concentrations throughout a 24-hour period. Although the secretion of other hormones may differ in older versus younger adults, whether the differences are truly age-related or are due instead to disease-related processes is difficult to establish. Endocrine diseases such as diabetes mellitus and thyroid disorders together affect about 12% of Americans. This chapter will focus on diabetes mellitus, obesity, thyroid disorders, sexual dysfunction, and other endocrine diseases in older adults.

Diabetes Mellitus

Etiology, Epidemiology, and Clinical Presentation in Older Adults

According to the Centers for Disease Control and Prevention, the prevalence of diabetes has risen to almost 27% of people 65 and older. Because its prevalence increases with advancing age, diabetes will become even more common with the aging of the American population. Interestingly, nondiabetic patients have been noted to have higher hemoglobin A1c (HbA1c) levels as they age. The HbA1c levels have been reported to increase 0.012% per year. Also, the prevalence of diabetes continues to rise among minority groups. Among older adults with diabetes, about 40% were diagnosed at 65 or older. Patients with type 1 diabetes have increased their life expectancy and, as a result, more older adults will have type 1 diabetes in the near future. Case reports of older adults diagnosed with type 1 diabetes have been published, although the true prevalence of type 1 diabetes in the older adults remains uncertain.

An estimated 35% of adults have prediabetes, and this estimate increases to more than 50% in individuals over 65 years of age.
Diabetes, both diagnosed and undiagnosed, is present in 8.3% of Americans. This figure increases to 26.9% among people over 65 (see Figure 10-1).\textsuperscript{4,9} The American Diabetes Association (ADA) recommends screening all adults over 45 for diabetes every 3 years. About 20% to 25% of patients in this age group have impaired glucose tolerance and a twofold increase in the risk of mortality from macrovascular complications.\textsuperscript{10} Older adults with diabetes, compared to individuals of the same age who do not have the disease, are two to three times more likely to report an inability to walk a quarter mile or to perform activities such as climbing stairs, using a cane or walker, or doing housework.\textsuperscript{9}

The etiology of type 2 diabetes includes both genetic and environmental factors, with obesity and physical inactivity comprising the latter group. Several genes have been identified as increasing the risk of developing type 2 diabetes independently of environmental factors.\textsuperscript{11} Predictors for the development of type 2 diabetes include a reduction in insulin secretion, insulin resistance, elevated body mass index (BMI), being a current smoker, and elevated liver enzymes.\textsuperscript{12} Insulin resistance is the result of increased inflammation secondary to high concentrations of free fatty acids and tumor necrosis factor-\(\alpha\), an increase in obesity, increasing age, and decreased physical activity.\textsuperscript{12} Several factors increase the likelihood of older adults developing type 2 diabetes. One age-related factor in diabetes is the alteration of insulin secretion in response to an oral glucose load.\textsuperscript{13} Older adults may also have an increase in insulin resistance due to central obesity, high saturated fat intake, and inactivity. The poor food choices in some older individuals may be due to financial stressors and an inability to chew certain foods. Research has identified differences between older obese and lean individuals. Although older adults with diabetes often have normal hepatic glucose production, lean older adults may have decreased insulin secretion but normal insulin-mediated glucose disposal.\textsuperscript{14} These patients have been referred to as having diabetes type 1½.\textsuperscript{14,15} Conversely, obese older adults with diabetes often have normal insulin secretion but increased insulin resistance.\textsuperscript{14}

Older adults with diabetes may not have the typical symptoms of hyperglycemia. As people age, the renal threshold for glucose increases and, as a result, older persons may not have the polyuria and nocturia that younger patients

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**Figure 10-1.** Estimated prevalence of diagnosed and undiagnosed diabetes in people age 20 years or older, by age group, United States, 2005–2008.

may experience. In addition, the normal thirst mechanism declines with advancing age. Older persons may have only vague symptoms of fatigue, weight loss, vision disturbances, urinary incontinence, or other symptoms that are easily mistaken for common comorbid conditions. Older adults with diabetes may have an abnormal random glucose as their only presenting sign of diabetes.

**KEY POINT:** Older patients often lack the classic symptoms of diabetes and instead present with urinary incontinence, confusion, and fatigue, which may be confused with other diseases.

### Summary of Standard Treatment

Based on the ADA clinical practice guidelines, the recommended optimal glycemic control for an adult with diabetes is to achieve an HbA\(_1c\) <7%; a less stringent goal of <8% may be appropriate for older patients. This would include preprandial glucose concentrations between 70 and 130 mg/dL and postprandial concentrations <180 mg/dL. Although a target HbA\(_1c\) of <6% may reduce some diabetes-related complications, the risk of hypoglycemia increases. Recent trials have shown that targeting HbA\(_1c\) to normal levels (below 6%) may increase the risk of cardiovascular complications as well as increased hypoglycemic episodes or have no significant benefit. The recommended goal blood pressure in patients with diabetes is <130/80 mmHg. Overall treatment should include medical nutrition therapy (MNT), metformin with lifestyle changes such as MNT and exercise, and early insulin initiation, if necessary. Table 10-1 summarizes the standard drug therapies for diabetes as well as other endocrine disorders.

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**Treatment Recommendations for Older Adults**

Potential quality-of-life issues for older adults with diabetes should be acknowledged when developing a treatment plan that may be complicated and expensive. An older person who is cognitively intact and otherwise independent in activities of daily living should have a target HbA\(_1c\) of <7%. Frail older persons with a life expectancy of <5 years or individuals at otherwise high risk of adverse outcomes from hypoglycemia may have a higher goal, such as an HbA\(_1c\) <8%, provided the risk of acute hyperglycemia is reduced.

The ADA recommends providing patients the estimated average glucose as well as the HbA\(_1c\) when reporting results to allow them to reflect on the similarity of blood glucose readings that they would do with home monitoring. The diabetic complication with the highest morbidity and mortality is cardiovascular disease. The 2013 updated American Geriatric Society Panel on Improving Care for Elders with Diabetes indicated that most older persons who have diabetes also benefit from treatment of their hypertension and dyslipidemia, if present. Aiming for systolic blood pressure of <130 mmHg does not have better cardiovascular outcomes compared to systolic blood pressure between 130 and 140 mmHg. The use of low-dose aspirin for primary prevention should also be considered on an individual basis.

**KEY POINT:** Older patients must have individualized treatment goals that take into consideration their life expectancy, comorbid conditions, level of frailty, acute risk of hypoglycemia, care setting, and quality-of-life issues.
### Table 10-1. Endocrine Treatments and Geriatric Considerations

<table>
<thead>
<tr>
<th>Medication Examples</th>
<th>General Adult Treatment Principles</th>
<th>Geriatric Considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Miglitol (Glyset)</td>
<td>Monotherapy adjunct to diet to improve glycemic control in type 2 diabetes. May be used in combination therapy with a sulfonylurea.</td>
<td>No specific trials in older adults have been conducted in patients on acarbose. Dosage adjustments not necessary. Elderly patients had 1.5 times serum concentrations compared to younger adults.</td>
</tr>
<tr>
<td>Acarbose (Precose)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Metformin (glucophage)</td>
<td>Monotherapy for type 2 diabetes or used concomitantly with a sulfonylurea or insulin to improve glycemic control.</td>
<td>AUC and half-life increased in elderly. Initial dose and maintenance dosing should be conservative. Should not titrate to maximum dosage. Not recommended to use in elderly patients (≥80).</td>
</tr>
<tr>
<td>Sitagliptin (Januvia)</td>
<td>Monotherapy for type 2 diabetes or in combination with other antidiabetic agents.</td>
<td>One clinical trial showed no difference in safety or efficacy compared to younger adults; less risk of hypoglycemia than other medications.</td>
</tr>
<tr>
<td>Saxagliptin (Onglyza)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Exenatide (Byetta)</td>
<td>Adjunctive treatment of type 2 diabetes in patients receiving sulfonylurea, metformin, or TZD or a combination of these medications.</td>
<td>Not recommended in patients with creatinine clearance &lt;30 mL/min; less risk of hypoglycemia than other medications.</td>
</tr>
<tr>
<td>Repaglinide (Prandin)</td>
<td>Monotherapy for type 2 diabetes or adjunctive therapy in patients on metformin or TZD.</td>
<td>No changes in safety and efficacy were seen in patients ≥65 on nateglinide. One trial showed that patients ≥65 taking repaglinide had less hypoglycemia compared to a sulfonylurea.</td>
</tr>
<tr>
<td>Nateglinide (Starlix)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Glyburide (Micronase, Diabeta)</td>
<td>Management of type 2 diabetes May be used as monotherapy or in combination with metformin or insulin.</td>
<td>Differences between each sulfonylurea. May cause rapid and prolonged hypoglycemia despite glucose administration. Use with caution in patients with renal insufficiency. Glipizide preferred because of fewer drug interactions and elimination is not dependent on renal function. Chlorpropamide and glyburide are not recommended in the elderly.</td>
</tr>
<tr>
<td>Glipizide (Glucotrol)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Glimepiride (Amaryl)</td>
<td></td>
<td></td>
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<tr>
<td>Chlorpropamide (Diabinese)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tolbutamide (Orinase)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tolazamide (Tolinase)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pioglitazone (Actos)</td>
<td>Monotherapy for type 2 diabetes or in combination therapy with sulfonylureas, metformin, or insulin. Rosiglitazone is not recommended in combination with insulin.</td>
<td>No dosage adjustments recommended with either rosiglitazone or pioglitazone; with rosiglitazone, may be an increased risk of fractures in hand, upper arm, and foot. Rosiglitazone should be used cautiously in patients with low bone density or history of fractures or falls.</td>
</tr>
<tr>
<td>Rosiglitazone (Avandia)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Various insulins</td>
<td>Treatment of type 1 or type 2 diabetes.</td>
<td>Initial doses may require consideration for renal function; elderly may need assistance to draw up insulin in a syringe due to dexterity and vision issues. May need to use prefilled syringes or pen devices; patient must recognize hypoglycemic and hyperglycemic symptoms.</td>
</tr>
</tbody>
</table>
Table 10-1. (cont’d)

<table>
<thead>
<tr>
<th>Medication Examples</th>
<th>General Adult Treatment Principles</th>
<th>Geriatric Considerations</th>
</tr>
</thead>
</table>
| Sodium-glucose cotransporter 2 inhibitors  
Canagliflozin (Invokana)  
Dapagliflozin (Farxiga) | Management of type 2 diabetes.  
Canagliflozin: Should not be used in patients with an estimated glomerular filtration rate (GFR) of <45 mL/min. If GFR = 45–60 mL/min, maximum dose is 100 mg daily.  
Dapagliflozin: Not recommended for use in patients with GFR <60 mL/min. | |

Drugs Used for Weight Loss/Control

| Orlistat (Xenical, over-the-counter Alli) | Used with reduced-calorie diet to promote and maintain weight loss.  
Contraindicated in cholestasis and chronic malabsorption syndrome.  
May interact with anticonvulsants, cyclosporine, levothryoxine, and warfarin. | Most studies excluded older adults.  
May cause or worsen fecal incontinence.  
May lead to deficiency of fat-soluble vitamins. |
| Lorcanerin (Belviq) | May interact with SSRIs, SNRIs, MAOIs, triptans, bupropion, dextromethorphan, and St. John’s wort.  
Risk of serotonin syndrome.  
Has not been studied in individuals using insulin. | Risk of cognitive impairment.  
Long-term effects on cardiovascular morbidity and mortality are unknown. |
| Phentermine and topiramate extended release (Qsymia) | Controlled substance.  
May interact with nonpotassium-sparing diuretics, and CNS depressants.  
Adverse effects include dizziness, insomnia, constipation, dry mouth, paresthesias, and dysgeusia. | Contraindicated in glaucoma, hyperthyroidism, with MAOIs.  
Risk of cognitive impairment, tachycardia, metabolic acidosis, increased serum creatinine.  
Long-term effects on cardiovascular morbidity and mortality are unknown. |

Drugs for Thyroid Disorders

| Methimazole (Tapazole)  
Propylthiouracil | Adverse effects include rash, urticaria, arthralgias, hepatotoxicity, and agranulocytosis (<0.5 %). | Older adults may be at increased risk of agranulocytosis. |
| Levotheroxine (Synthroid, Tirosint)  
Triiodothyronine (Cytomel)  
T3 and T4 (Lioitrix)  
Dessicated thyroid (Armour thyroid) | Levotheroxine (T4) preferred because of its stable conversion to T3 and half life of 4–7 days. T3 has a shorter half-life and requires multiple daily dosages.  
Combination T3 and T4 products are more expensive and require monitoring of both T3 and T4 concentrations, unlike levotheroxine preparations.  
Dessicated thyroid has had standardization problems as well as adverse cardiac effects. | Primary concern is the precipitation of cardiac events when beginning replacement therapy.  
Dosages should be started low (i.e., levotheroxine 12.5–25 mcg once daily) and gradually titrated upward, especially in presence of known CVD. |
Individualization of Treatment in Type 2 Diabetes

Treatment of older adults with diabetes is similar to that of younger patients and involves the same stepwise approach.19,20 Nonpharmacologic treatments (e.g., diet and exercise) should be tailored to the individual. An older adult who is malnourished will need adequate calories and protein. The presence of comorbid conditions such as severe cardiovascular disease and mobility problems will require careful consideration in the development of an exercise plan. An interdisciplinary team that includes a dietitian or nutritionist, as well as a physical therapist, is important in developing an optimal care plan.

The selection of drug therapy requires consideration of goals and the presence of comorbid conditions, especially in the frail individual (see Table 10-2). A primary consideration in selecting drug therapy is the risk of hypoglycemia, such as a patient with impaired kidney function or inconsistent oral calorie intake. A patient with cognitive impairment may not be able to communicate symptoms of hypoglycemia. Other considerations include life expectancy, baseline glycemic control, adverse effects, tolerability, and previous diabetes medication use.19 For example, an older adult with previous falls and hospital admissions secondary to sulfonylurea therapy should be switched to drugs with a lower potential for hypoglycemia. Biguanides, thiazolidinediones, alpha-glucosidase inhibitors, glucagon-like peptide-1 receptor agonists (GLP-1 agonists), sodium-glucose cotransporter 2 inhibitors, and dipeptidyl peptidase IV inhibitors generally do not cause hypoglycemia unless used in combination with drugs that stimulate insulin release.21,22

Diabetes mellitus generally requires additional medications over time to maintain glycemic control. Additional medications should be considered within 2 to 3 months after initiation of a therapy or any time that the HbA₁ₑ is not at an individual’s goal. Lifestyle interventions are essential and may significantly decrease hyperglycemia.23 Implementing lifestyle changes such as weight loss and exercise programs may also improve hypertension and dyslipidemias. Lifestyle recommendations must be tailored to the individual’s functional status, level of frailty, and comorbid conditions. The risks of exercise in older patients may include musculoskeletal injuries or worsening foot ulcers or wounds, so the exercise plan should be carefully developed.

Common Oral Medications

Along with lifestyle interventions, metformin is the preferred initial therapy for type 2 diabetes. The
## Table 10-2. Comparison of Pharmacotherapy Options for Type 2 Diabetes in Older Adults

<table>
<thead>
<tr>
<th>Medication</th>
<th>Advantages</th>
<th>Disadvantages</th>
</tr>
</thead>
<tbody>
<tr>
<td>Metformin</td>
<td>Hypoglycemia (adverse effect) usually does not occur if monotherapy</td>
<td>Generally, should not be dosed to maximum in older adults</td>
</tr>
<tr>
<td></td>
<td>May help with weight loss</td>
<td>Gastrointestinal side effects may be common</td>
</tr>
<tr>
<td></td>
<td>May be beneficial to lipid profile</td>
<td>Rare risk of lactic acidosis</td>
</tr>
<tr>
<td></td>
<td>Available as a generic drug</td>
<td>Should not use in patients with moderate-severe heart failure because of risk of lactic acidosis</td>
</tr>
<tr>
<td></td>
<td>May improve insulin resistance</td>
<td></td>
</tr>
<tr>
<td>Sulfonylureas</td>
<td>Least expensive, available generically</td>
<td>High risk of hypoglycemia</td>
</tr>
<tr>
<td></td>
<td>Works well in lean patients</td>
<td>Weight gain</td>
</tr>
<tr>
<td>Thiazolidinediones</td>
<td>No hypoglycemia if monotherapy</td>
<td>Weight gain</td>
</tr>
<tr>
<td></td>
<td>Improves insulin resistance</td>
<td>Edema</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Expensive</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Increased risk of fractures of the hand, upper arm, and foot</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Risk of cardiovascular events with rosiglitazone</td>
</tr>
<tr>
<td>Alpha-glucosidase inhibitors</td>
<td>No hypoglycemia if monotherapy</td>
<td>High incidence of gastrointestinal side effects</td>
</tr>
<tr>
<td></td>
<td>No weight gain</td>
<td>Hypoglycemia must be treated with dextrose or lactose</td>
</tr>
<tr>
<td></td>
<td>Lowers postprandial glucose levels</td>
<td>Weak, lowers HbA₁c 0.5%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Must be dosed prior to each meal</td>
</tr>
<tr>
<td>Meglitinides</td>
<td>Slight decreased risk of hypoglycemia compared to sulfonylureas</td>
<td>Expensive</td>
</tr>
<tr>
<td></td>
<td>Reduces postprandial glucose levels</td>
<td>Risk of hypoglycemia</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Must be taken with each meal; multiple doses</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Weight gain</td>
</tr>
<tr>
<td>Dipeptidyl peptidase IV inhibitors</td>
<td>No hypoglycemia if monotherapy</td>
<td>Use with caution in renal impairment</td>
</tr>
<tr>
<td></td>
<td>Few side effects</td>
<td>Weak, lowers HbA₁c 0.5%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Expensive</td>
</tr>
<tr>
<td>Incretin mimetics</td>
<td>No hypoglycemia if monotherapy</td>
<td>Injectable</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Nausea, vomiting</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Expensive</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Should not use in patients with creatinine clearance &lt;30 mL/min</td>
</tr>
<tr>
<td>Amylin analog</td>
<td>Effective at lowering blood glucose levels</td>
<td>High risk of hypoglycemia</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Must be used with insulin</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Expensive</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Injectable</td>
</tr>
<tr>
<td>Bromocriptine</td>
<td>No hypoglycemia if monotherapy</td>
<td>Weak</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Expensive</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Hypotension may occur</td>
</tr>
</tbody>
</table>
drug decreases hepatic glucose production and increases insulin sensitivity. In general, metformin is well tolerated if titrated slowly upward. The drug has the potential advantage of causing weight loss, which may benefit the lipid profile. In addition, a systematic review indicated that the use of metformin may decrease the risk of cardiovascular mortality in older adults.7

Several precautions exist when using metformin in older adults (Table 10-2). Metformin may have a reduced total body clearance and has a prolonged half-life in older patients. Data obtained from relatively younger subjects have shown that metformin may be used until the glomerular filtration rate falls below 30 mL/min.21,24,25 Although clinically significant responses to metformin usually occur at dosages over 1500 mg daily, the dosage should not be increased to the maximum because of the potential risk for lactic acidosis in older adults with impaired kidney function. Metformin should be used only after careful calculation of the creatinine clearance and after ensuring that it is >30 mL/min.21 Dosages should be titrated more slowly than in younger adults to lessen the loss of appetite, stomach upset, and diarrhea to which older adults may be more sensitive. In addition, a study of older adults comparing glipizide and metformin showed that, while the drugs were equally effective, metformin caused weight loss, whereas glipizide caused weight gain.26 Vitamin B12 deficiency is associated with chronic metformin use in older adults due to its effect on ileal absorption of the vitamin; its use may be overlooked as a potential contributing factor for vitamin B12 deficiency and should be supplemented with B12 injections as compared to oral therapy.27

**KEY POINT:** Patients should begin diabetes control with lifestyle changes, individualized to their own needs, and then start metformin therapy if their kidney function is adequate.

First- and second-generation sulfonylureas are equally effective and are available as generic drug products. In general, glyburide, glipizide, and glimepiride are preferred. Glyburide may accumulate in impaired kidney function; a meta-analysis comparing glyburide with other secretagogues showed an increased risk of hypoglycemia with the drug.28,29 Patients should be started on the lowest dose, such as glipizide 2.5 mg per day, and increased by 2.5–5 mg every 1–2 weeks. Some first-generation sulfonyl-
ureas require more frequent dosing and others have longer half-lives, such as chlorpropamide, which significantly increases the risk of hypoglycemia. These drugs are not optimal choices for older adults with diabetes.

The thiazolidinediones (TZDs), pioglitazone and rosiglitazone, act by improving insulin resistance. Pioglitazone is preferred because rosiglitazone has been shown to increase the risk of myocardial infarction (MI) but not increase the risk of cardiovascular mortality or death from other causes.\(^{30,31}\) The use of rosiglitazone should be avoided in older adults because of the higher prevalence of cardiovascular diseases, such as MI and heart failure. Pioglitazone is effective in the treatment of type 2 diabetes in older adults and may also have a beneficial effect on lipids. Pioglitazone should be started at a dosage of 15–30 mg per day and titrated to a maximum of 45 mg daily. The beneficial effects of pioglitazone may take at least several weeks. Adverse effects with TZDs include weight gain, edema, osteopenia that could lead to fractures, and a twofold increase in the risk of heart failure. These drugs should generally be avoided in older adults with heart failure.\(^{21}\)

**KEY POINT:** Maintenance dosages of sulfonylureas in older adults should be on the lower end of the recommended range because of both pharmacokinetic and pharmacodynamic alterations affecting outcomes with these drugs.

**Insulin**

If a patient’s diabetes does not respond to combinations of oral medications, insulin should be considered. In the past, the initiation of insulin was delayed for years after diagnosis or for very poor glycemic control. Often, insulin is deferred because of a perception that older adults are unable to manage this therapy. Insulin can be used safely in older adults by initiating the therapy slowly and titrating carefully. Treatment with insulin and additional medications are now recommended within 2–3 months of failed monotherapy.\(^{21}\) Newer basal insulin products such as insulin glargine may have advantages in older adults, but they have not been studied in these patients.

Basal insulin may be added to oral combination therapy in older adults. For example, intermediate-acting neutral protamine Hagedorn (NPH) insulin may be initiated at 10 units daily in addition to combination treatment with metformin and glipizide. The insulin dosage can be titrated up by 1–2 units every 3 days to avoid hypoglycemia and maintain premeal and bedtime blood glucose concentrations of 80–140 mg/dL. Although titrating insulin NPH to achieve an HbA\(_1c\) of <7% may take several weeks to months, an HbA\(_1c\) of <8% may be achieved sooner. Basal or bolus insulin can be added to the regimen with continued monitoring.\(^{21}\) If basal insulin therapy becomes inefficient or the targets are not achievable, the patient may alter his or her insulin regimen with basal and bolus combinations in fixed regimens (i.e., insulin 70/30 twice daily therapy) or multiple daily doses of insulin (i.e., insulin glargine daily with mealtime boluses of insulin lispro). Monitoring hypoglycemia is especially important in older adults because hypoglycemia may increase risk of falls.

**KEY POINT:** Insulin treatment should be considered when the HbA\(_1c\) remains above the desired goal despite combination therapy with the recommended dosages.

Assistive devices for insulin therapy may help older patients with vision, hearing, and dexterity problems successfully manage their therapy. One product attaches to an insulin syringe to magnify the markings on the syringe for those with impaired vision. Insulin pen devices have also made insulin delivery easier for individuals who are visually impaired or who have dexterity problems, although even pen devices may still be difficult to manage. For frail skin, shorter pen needles are available and do
not require pinching up of the skin. Although no insulin pen devices are specifically promoted for individuals who are visually impaired, patients can be trained to use these devices successfully if they are provided with appropriate opportunities to practice their use. A product called Count-A-Dose attaches up to two vials of insulin and uses a low-dose syringe (<50 units). The product clicks with each unit of insulin withdrawn from the vial and also allows for mixing different types of insulin.

**Adjunctive Medications**

Other medications may be used as adjunctive therapies, although they have not been well studied in older adults. The primary goal of adding these medications to existing regimens is to control blood glucose with little or no hypoglycemia or other adverse effects. Clinicians should recognize that many older adults may have a limited income; each additional medication should be evaluated for cost, ease of use, adverse effects, and actual effects on glycemic control.

Meglitinides, including repaglinide and nateglinide, are similar to the sulfonylureas and stimulate beta cells to increase insulin secretion, although they bind to a different receptor. These drugs have a shorter half-life than sulfonylureas and should be dosed with meals. The primary benefit of the meglitinides is that the risk of hypoglycemia is lower because patients take the medication only if they are eating food containing carbohydrates, and they may skip doses if they are not eating.

Alpha-glucosidase inhibitors, such as acarbose and miglitol, slow polysaccharide absorption in the brush border of the small intestine. Glucose absorption is delayed, thereby lowering postprandial glucose concentrations; the HbA1c level is lowered by 0.5%. The medication should be used cautiously in patients with serum creatinine >2 mg/dL even though <2% of the drug is absorbed. The initial dosage of acarbose should be 25 mg three times a day with the first bite of each meal. If the patient forgets to take acarbose with the first bite of the meal, he or she should skip that dose. Increased gas and belching occur in 25% to 45% of patients. Patients who become hypoglycemic while taking a combination of antidiabetic drugs that include acarbose or miglitol should be advised to take glucose tablets or skim milk, and not sucrose products such as orange juice. This can be an important counseling point in long-term care environments where nursing protocols may include orange juice as an intervention for hypoglycemia.

The GLP-1 agonists are produced by the L-cells in the small intestine and enhance glucose-stimulated insulin secretion. Exenatide and liraglutide are analogs of GLP-1 and have a longer half-life than the naturally occurring peptide. Exenatide slows gastric motility and suppresses the secretion of glucagon. Although hypoglycemia does not occur, gastrointestinal symptoms such as nausea, vomiting, and diarrhea may develop. Patients taking GLP-1 agonists may decrease their nausea by ingesting smaller meals. The nausea from GLP-1 agonists may also be due to previously unrecognized diabetic gastroparesis. The initial dosage of exenatide is 5 mcg injected subcutaneously twice daily and slowly titrated after a month to a maximum of 10 mcg twice a day prior to meals. The long-acting exenatide is dosed 2 mg once weekly and is dispensed in a reconstituted kit. This formulation requires multiple steps and adequate hand strength to administer, which may be difficult in some older adults. Although studies of exenatide have enrolled older adults, its use in this patient group has not been specifically evaluated. Liraglutide is dosed 0.6 mg subcutaneously once daily and may be increased to 1.2 mg or 1.8 mg daily. The effects of liraglutide on cardiovascular outcomes are being evaluated in an ongoing trial.

The amylin agonist, pramlintide, is dosed three times daily before meals in patients using mealtime insulin. The drug inhibits glucose-dependent glucagon secretion and slows gastric emptying, ultimately lowering postprandial glucose values. Adverse effects include nausea, anorexia, and weight loss. Severe hypoglycemia may occur if the insulin dosage
is not halved when pramlintide is first started. Pramlintide is usually dosed 60–120 mcg subcutaneously prior to meals in patients with type 2 diabetes.

The dipeptidyl peptidase-IV (DPP-IV) enzyme rapidly breaks down GLP-1 and glucose-dependent insulinotropic peptide (GIP). Sitagliptin, saxagliptin, alogliptin, and linagliptin are DPP-IV inhibitors which enhance the activity of GLP and GIP. Although well tolerated, the HbA1c is only lowered by 0.6% to 0.9%. The dosing of DPP-IV inhibitors in older adults is the same as the usual adult dosing, although alogliptin, sitagliptin, and saxagliptin require a dosage reduction as the creatinine clearance declines. For example, sitagliptin is dosed 100 mg once daily, but if creatinine clearance is between 30 to 50 mL/min, dosage should be 50 mg daily and <30 mL/min at 25 mg daily. Hypoglycemia was three times lower in older adults treated with DPP-IV inhibitors compared to those receiving conventional oral antihyperglycemic agents.

Although not preferred drugs, colesevelam and bromocriptine have a labeled indication lowering blood glucose in type 2 diabetes. The use of colesevelam in older adults may improve lipid and glucose concentrations and with good adherence might reduce the risk of acute MI and stroke. The most common adverse effect of colesevelam is constipation, which can be a concern in the elderly. Bromocriptine may reduce HbA1c by 0.5%. Although the mechanism of action is unknown, bromocriptine may affect the circadian rhythm, subsequently helping to reduce obesity and insulin resistance. Older adults should use the drug cautiously because of potential drug interactions, symptomatic hypertension, and an unknown effect of impaired kidney function.

Sodium-glucose cotransporter 2 (SGLT2) inhibitors such as canagliflozin work by inhibiting the reabsorption of glucose in the proximal renal tubules. This lowers the renal threshold for glucose, resulting in increased urinary excretion. Canagliflozin is dosed 100 mg daily prior to the first meal of the day and may be increased to 300 mg if the creatinine clearance is >60 mL/min. Patients with renal impairment of 45 mL/min to <60 mL/min should take a maximum of 100 mg daily; in the presence of a creatinine clearance <45 mL/min, the drug should not be used. Although well tolerated in some studies, older adults are at higher risk of hypotension, dizziness, urinary tract infection, and dehydration due to intravascular volume depletion from canagliflozin.

Special Considerations in Older Adults

Team Approach

Patients with diabetes should be managed using an individualized team-based approach that includes physicians, pharmacists, nurses, and dietitians, among others. All patients need education about their disease as well as problem-solving skills to manage their diabetes on a day-to-day basis. A patient’s age, activity level, eating patterns and preferences, dental issues, cultural and social factors, personality, financial situation, eyesight, and other medical conditions should be considered in developing an individualized care plan. Collaboration between the patient, family or other caregivers, and health professionals is essential for optimal care.

Comprehensive Care

Older adults with diabetes are a heterogeneous group. Although some may have had diabetes for several years with mild-to-severe microvascular and macrovascular complications already present, other individuals may have just been diagnosed with diabetes and have no complications. According to the ADA and the American Geriatrics Society clinical practice guidelines, frail patients and patients who have complications that lead to shortened life expectancy should have a less intensive HbA1c goal. Even if the therapeutic plan does not include tight control of blood glucose, other conditions should be assessed independently from this decision. For example, aggressive treatment with
moderate- to high-intensity statins in diabetes patients age 40 to 75, or anticoagulation in atrial fibrillation, may be appropriate even if the HbA1c target for a patient is 8%. Another example is control of hypertension, which has demonstrated benefit in healthy older adults with diabetes. In the Systolic Hypertension in the Elderly Program trial, older persons with diabetes and isolated systolic hypertension treated with antihypertensive therapy had a significantly decreased risk of coronary events compared to their nondiabetic counterparts. In addition, older persons often have more disability because of their diabetic complications, which may lead to depression in patients over 55 with diabetes. Their depression should be managed aggressively.

In managing diabetes in older adults, the effect of concomitant diseases and drug therapy, vision and hearing problems, poor nutritional intake, and financial issues related to medications and other diabetic supplies should be carefully considered as well as cognitive problems and depression. A frail older adult with unrecognized cognitive impairment who is living alone will have difficulty adhering to complicated lifestyle interventions and complex drug regimens. Also, adults age 18–44 with diabetes have a 15% prevalence of blindness, whereas 27% of adults 75 and older with diabetes are blind. The management of diabetes requires patients to have adequate vision and dexterity to use devices such as an insulin syringe and a glucometer for self-monitoring of blood glucose concentrations. Drawing up insulin from a vial requires adequate vision to accurately read the markings on the syringe. Dexterity is also important for insulin administration and blood glucose monitoring, which requires fine motor skills and dexterity to get test strips out of storage vials. Even the simple act of recording blood glucose concentrations in a logbook requires dexterity, vision, adequate cognition, and other steps to successfully accomplish the task.

A pharmacist can provide patient counseling or assessment of self-administration abilities as well as support caregivers who provide insulin administration assistance. In the long-term care setting, the consultant pharmacist’s observance of an “insulin pass” by the nursing staff is one way of providing ongoing quality assurance regarding administration procedures.

### Blood Glucose Monitoring

Self-monitoring of blood glucose is recommended for all patients who have been prescribed an intensive insulin regimen consisting of multiple injections per day. In other patients, self-monitoring of blood glucose is an important tool in managing the disease. Although improved glycemic control has not been consistently demonstrated in studies, blood glucose monitoring in the older adult might help to improve long-term outcomes and prevent hypoglycemic reactions.

The preferred frequency and timing of blood glucose measurements in older adults is not known, so individual patients should be assessed to evaluate their interest and abilities. As the diabetes therapy intensifies, blood glucose monitoring should also be increased, either by the patient or a qualified caregiver. Fasting blood glucose at pre-lunch, pre-dinner, and pre-bedtime intervals can be checked. If a patient is able to adhere to, or cooperate with, an intensive monitoring schedule, this provides the safest oversight of therapy outcomes. However, depending on the situation there are many instances in which more intensive monitoring is not feasible. For instance, in the care of individuals with dementia, finger stick monitoring can be a source of significant agitation and distress. In any circumstance where medication or insulin management is deemed medically necessary but a reduction in monitoring intensity is desired, a pattern management approach is one strategy that can achieve this while still yielding good information about glucose control over time. For example, once a reasonably predictable pattern of blood glucose control is established using a regimen of four assessments per day, this can be divided in half by testing twice daily for 3 days in the morning and pre-dinner, and then twice daily for another 3 days before lunch and at bedtime.

Those patients with Medicare will be able to obtain diabetes test strips if they are diagnosed
with diabetes. The amount that Medicare covers will vary depending on whether the patient is on insulin. Many third-party payers will only cover 300 test strips and lancets every 3 months for patients who use insulin; noninsulin-dependent patients can get 100 test strips and lancets every 3 months. Patients who are taking medications that increase insulin secretion, such as sulfonylureas, meglitinides, or insulin, may require more testing than patients receiving other therapies. Frail older adults are at an increased risk of severe hypoglycemia, and blood glucose monitoring by caregivers may reduce this risk.

Blood glucose monitors help to improve a patient’s autonomy in his or her diabetes management. All patients should be shown how to use their glucose monitors and have routine follow-up to ensure proper technique. However, the use of glucose monitors can be difficult for patients who have cognitive or visual impairment or dexterity problems. Blood glucose monitors vary in size, amount of blood needed for obtaining sample, visual acuity required to perform the test, dexterity required to handle test strips and supplies, and cognitive ability required to accomplish a successful test. Some glucose monitors are able to “talk” to patients to assist them in testing their blood glucose (e.g., Prodigy®). Other systems also help patients maintain independence in their diabetes self-care.

For older patients with good vision, but dexterity problems, several glucose meters can be used. Test strips for glucose meters are small and removing them from the vial to insert into the meter can be difficult if the patient has arthritis of the hands. Some glucose monitors have cartridge or drum systems that contain several test strips in a disk and allows for multiple tests to be done (i.e., Accu-Chek Compact®). Coding the meter, code keys, and setting meters can also be difficult. Several meters do not require changing codes or code keys, which allows patients to test their blood glucose with fewer steps.

Ongoing self-management of diabetes is a key component in the successful treatment of the disease. Many older adults with diabetes, either newly diagnosed or those with long-standing disease, will have challenges in managing their diabetes. Health professionals, particularly pharmacists, must be aware of these barriers and be able to offer potential strategies for overcoming the specific challenges.

**Prevention of Diabetes-Related Complications**

A primary goal in treating diabetes is to prevent the long-term complications of cardiovascular disease, nephropathy, retinopathy, neuropathy, impaired wound healing, and dental disease. The long-term complications may or may not be relevant to a newly diagnosed older adult with diabetes, given the patient’s predicted life expectancy. Few large placebo-controlled prospective studies of diabetes have enrolled older adults. The United Kingdom Prospective Diabetes Study (UKPDS) examined the effect of different treatments on the chronic complications from type 2 diabetes mellitus in patients 25 to 65 years old. As a result, the findings from UKPDS are difficult to apply to frail individuals in their 80s or older.

The Action to Control Cardiovascular Risk in Diabetes (ACCORD) trial randomized patients between the ages of 40 and 79 into either intensive glucose control (targeting HbA1c <6%) or standard treatment (HbA1c 7% to 7.9%). The mean age of participants was 62. The primary and secondary outcomes of the ACCORD trial were nonfatal MI, nonfatal stroke, death from cardiovascular causes, or death from any cause. Overall, the primary and secondary outcomes were increased in patients receiving intensive treatment compared to the group receiving standard therapy. The worst outcomes in the intensive group may have been due to the rapidity of the decrease in blood glucose concentrations early in therapy. Hypoglycemia requiring medical assistance was three times higher in the group receiving intensive versus standard therapy. A significant weight gain of 10 kilograms occurred twice as frequently in the group receiving intensive therapy. Although older
adults were enrolled in this study, few participants had common concomitant diseases, such as heart failure, or were otherwise frail.

Participants in the Action in Diabetes and Vascular Disease: Preterax and Diamicron in Controlled Evaluation (ADVANCE) trial had a mean age of 66 years and only included patients over 55. This study evaluated whether intensive management of blood glucose versus standard treatment decreased microvascular or macrovascular outcomes. Primary outcomes were composites of macrovascular and microvascular events, and secondary outcomes included death from any cause, death from cardiovascular causes, and major coronary events. The outcome was not influenced by age.

Diabetic nephropathy is the leading cause of end-stage kidney disease and is increased in patients who have microalbuminuria. Several trials have demonstrated the benefit of reducing nephropathy in patients with type 2 diabetes. The ADVANCE trial showed a 21% relative risk reduction of nephropathy in patients intensively managed using sulfonylureas and other medications; the average age of participants was 66. The presence of microalbuminuria should be tested in all patients at the time of diagnosis of type 2 diabetes and annually thereafter.

An estimated 60% of patients with type 2 diabetes and proteinuria will also have retinopathy. Patients with newly diagnosed type 2 diabetes should have a dilated eye exam immediately and annually thereafter. Older adults with diabetes and nephropathy are also likely to have dental disease and peripheral neuropathy. Appropriate dental care for older adults with diabetes should include brushing teeth twice daily and flossing every day. Patients with diabetes should visit their dentist every 6 months for routine scaling and check-up. Note that many older adults will not have insurance for dental care, and in the nursing home setting, appropriate dental monitoring may be difficult to obtain.

Complications from neuropathies are common in older adults and are often undertreated. Older adults should be assessed at diabetes diagnosis and periodically thereafter. They should be asked about pain, as well as descriptive words to help assess the patient. Some cultures may not use words such as pain, but rather discomfort or “aching in legs.” Postural hypotension from autonomic neuropathies and weakness secondary to peripheral neuropathies can lead to falls in older adults. Although low-dose tricyclic antidepressants, anticonvulsants, and other medications treat peripheral neuropathies, adverse effects commonly occur in older adults. Adverse effects may include fatigue, urinary retention, dizziness, constipation, delirium, and confusion. Treatment options for peripheral neuropathy are discussed more fully in Chapter 13.

**Hypoglycemia**

Hypoglycemia is a potentially dangerous adverse effect in any patient with diabetes. Although hypoglycemia is usually mild and includes symptoms of shakiness, nervousness, dizziness, sweating, weakness, and confusion, a loss of consciousness may occur. Older adults may lose the ability to feel certain symptoms of hypoglycemia; they can be educated to recognize symptoms such as sweating, weakness, and fatigue. They or their caregivers should be encouraged to test their blood glucose when feeling these symptoms. Patients should also be encouraged to wear medical identification and carry glucose tablets or other 15-gram carbohydrate sources.

Cognitive impairment often prevents an individual from being able to articulate symptoms of hypoglycemia. In long-term care settings, regular blood glucose monitoring should be coupled with monitoring of dietary intake patterns. Facility protocols should include orders for hypoglycemia interventions, including parameters instructing the nursing staff when to react.

Most studies of diabetes and hypoglycemia have excluded older adults. In one trial, severe hypoglycemia requiring hospitalization was evaluated in patients over 80 with type 2 diabetes.
Most patients had several comorbid conditions and the HbA1c averaged 5.1%, indicating very tight control. Almost 75% of patients had been prescribed glyburide, and only a few were regularly self-monitoring blood glucose concentrations. This study indicated that older adults who are aggressively managed are likely to experience severe hypoglycemia requiring hospitalization. Older patients who are taking medications that can cause hypoglycemia should be closely monitored and have their medication dosages adjusted when the HbA1c is within target range.49

Another trial examined the risk of sulfonylureas and insulin in causing severe hypoglycemia in older adults. Combining both treatment groups, the incidence of severe hypoglycemia was 2 per 100 person-years, which would indicate a certain safety in treating older adults with hypoglycemic agents. The patients who were at a higher risk of developing severe hypoglycemia were the very elderly, patients who were frequently admitted to the hospital, and those patients with multiple medications.50 If a patient is likely to have hypoglycemia, he or she should have a less stringent HbA1c goal of <8%.

**Hyperosmolar Hyperglycemic Nonketotic Syndrome**

In contrast to diabetic ketoacidosis, which is more common in type 1 diabetes, hyperosmolar hyperglycemic nonketotic syndrome (HHNS) is more common in adults with type 2 diabetes and has a peak incidence in the seventh decade of life. Patients who develop HHNS have severe hyperglycemia and dehydration as well as increased serum osmolality. Individuals who have dementia are at the highest risk of developing HHNS.51 Older patients presenting with HHNS often have other acute conditions such as pneumonia, pancreatitis, and cardiovascular events. They may have had a severe osmotic diuresis, and their dehydration is due to both extracellular and intracellular water loss.51 Fluid replacement can be initiated with 0.9% NaCl until vital signs have stabilized, and then switched to 0.45% NaCl. A regular insulin bolus of 10–15 units followed by continuous infusion of 0.1 unit/kg/hr should be also initiated. Frequently patients who present with HHNS may be managed on oral agents when they are discharged from the hospital.51

**Obesity**

The prevalence of obesity in older adults has been increasing, and data from 2007–2008 indicate that 37.1% of men and 33.6% of women 60 and older were obese.52 Body weight usually peaks in middle age, stabilizes around ages 65 to 70, and then may decline slightly after age 70 until the end of life.53,54 Age-related increases in body fat may be due to a decrease in total energy expenditure.53,55 In addition, older adults may experience a decrease in lean body mass, some loss of height due to skeletal disorders, and a decrease in total body water.54 Although BMI is used to indicate whether an individual is overweight or obese, waist circumference may be a better indicator of obesity in this age group.53,54

**Benefits of Weight Loss**

Obesity is associated with poor quality of life, chronic illness, functional disability, and loss of independence.53,54 Older adults who are obese are at a greater risk of morbidity as well as osteoarthritis, obstructive sleep apnea, and cardiovascular disease; also, frailty may be worsened.53 Weight loss has the potential to improve these conditions, lessen depression, and increase quality of life.54 The onset of type 2 diabetes in obese individuals with impaired glucose tolerance may be delayed or prevented by weight loss.54,56 The Diabetes Prevention Program has indicated that simply a 5% weight loss may decrease the 5-year risk of developing diabetes by more than 50%.56 Weight loss is recommended by the American Society for Nutrition and the Obesity Society for older adults who are obese and have risk factors such as functional impairment and/or medical complications.53 Longevity and quality of life for an individual older adult should be considered when making this decision.
Risks of Weight Loss

Risks associated with weight loss include decreased bone mineral density and increased risk of osteoporosis and fractures. Increased mortality, frailty, decreased muscle mass, and vitamin deficiencies may also result. Consequently, older adults should discuss their weight with a healthcare professional to create an appropriate weight-loss plan. In addition, concomitant diseases and medications may have contributed to obesity and should be assessed. For example, patients taking insulin or sulfonylureas for type 2 diabetes may gain weight. Uncontrolled or undiagnosed hypothyroidism may increase weight, which may be treated with thyroid hormone, although thyroid hormone would be an inappropriate obesity treatment in euthyroid patients.

KEY POINT: Before beginning a weight-loss program, older adults should carefully consider the risks and benefits.

Nonpharmacologic Options

A combination of caloric reduction (also called energy restriction), exercise, and behavioral therapy are best for safe and effective weight loss in older adults. Behavioral therapy includes self-monitoring, goal-setting, social support, and stimulus control. Although behavioral therapy involves minimal risk and is effective for weight loss, it remains underused. The 2003 U.S. Preventive Services Task Force guidelines state that all adults should be screened for obesity and offered weight-loss counseling if obese. Yet only 44.5% of adults ages 60–69 and 32.4% of adults ages 70 and older who are obese reported receiving weight-loss counseling.

Regular exercise has many potential benefits. Flexibility and range of motion can be improved, as well as concentration and ability to manage stress. Independence may be maintained or increased, and endurance and functional capacity may be improved. A review of 14 randomized, controlled trials evaluated the effects of energy restriction, energy restriction plus aerobic training, energy restriction plus resistance training, or energy restriction plus a combination of aerobic training and resistance training on body mass and body composition. The trials ranged from 3 to 12 months in duration. The age range of participants was 51–70 years, and BMI range was 30.9–37 kg/m². Some studies showed positive results for cardiorespiratory fitness and muscle strength, in addition to decreases in body mass. The 12-month study demonstrated that energy restriction decreased body mass by 7.1 kg, and energy restriction plus exercise decreased it by 8.9 kg. Energy restriction was not found to prevent the age-related decrease in lean body mass.

Bariatric surgery is an effective procedural option, although the long-term benefits in older adults are unclear. A review of randomized, controlled trials with adults 60 years and older with a BMI of 30 kg/m² or greater found that bariatric surgery was lacking evidence of effectiveness. The best candidates for bariatric surgery include those individuals who are morbidly obese (BMI 35.0–39.9 kg/m²) and have at least one medical complication associated with obesity, such as heart failure, hypertension, type 2 diabetes, or sleep apnea. In addition, individuals with a BMI of 40 kg/m² and a low probability of success with other weight-loss options may be candidates.

Standard Adult Therapy

Three medications have a labelled indication for weight loss. These drugs include orlistat, lorcaserin, and combination phentermine and topiramate. At present, the evidence supporting the use of these drugs to treat obesity in older adults is limited.

Orlistat is a reversible inhibitor of gastrointestinal lipase and is used in combination with a reduced-calorie diet. Individuals taking orlistat are advised to reduce their fat intake to 30% or less of their total caloric intake. Most studies of orlistat excluded older adults or did not analyze results by age group if older adults
were included.\textsuperscript{52} Orlistat may reduce the ability to absorb fat-soluble vitamins. In addition, the drug may cause fecal incontinence, for which many older adults are already at risk because of age-related changes in sphincter function.\textsuperscript{53}

Lorcaserin is a serotonin 2C receptor agonist that is used as an adjunct to a reduced-calorie diet and increased exercise. Unlike older nonselective drugs in this class, lorcaserin has not demonstrated valvular heart disease after 2 years of use.\textsuperscript{56} Lorcaserin is indicated for patients with a BMI of 30–45 kg/m\textsuperscript{2} or a BMI 27–29.9 kg/m\textsuperscript{2} with hypertension, dyslipidemia, cardiovascular disease, impaired glucose tolerance, or sleep apnea. Data on its use in individuals over 65 years are not available.\textsuperscript{56} The efficacy and safety of lorcaserin has been studied in patients who have type 2 diabetes versus placebo.\textsuperscript{58} The average patient included was 52.7 years, female, white, had a BMI of 36 kg/m\textsuperscript{2}, and is taking metformin and a sulfonylurea. Lorcaserin reduced body weight up to 5.5%, and decreased HbA\textsubscript{1c} up to 1.9%.\textsuperscript{58}

Phentermine and topiramate extended release is an adjunct to a reduced-calorie diet and increased exercise. The combination has been studied in patients age 18–70, although <10% of patients were 65 or older and no patient was older than 70.\textsuperscript{59,60} Patients had a BMI of 27–45 kg/m\textsuperscript{2} and two or more comorbid conditions.\textsuperscript{60} On average, patients were 51 years old, female, white, with an average baseline weight of 102 kg, a BMI of 36 kg/m\textsuperscript{2}, an HbA\textsubscript{1c} of 5.9%, and a history of hypertension and/or metabolic syndrome.\textsuperscript{59,60} Both studies demonstrated statistically significant differences in the percentage of patients who achieved a 5% and a 10% reduction in weight after 1 and 2 years of use.\textsuperscript{59,60} Renal dosing is used for patients with CrCl <50 mL/min. Common adverse effects include insomnia and paresthesias. A dose-related increase in resting heart rate has been observed (>20 beats per minute), although its clinical significance is unclear.

**KEY POINT:** Evidence for efficacy and safety of weight-loss drugs in older adults is limited. All agents should be used with lifestyle changes to achieve the best results.

**Evidence for Pharmacologic Therapy in Older Adults**

Clinically significant changes in body weight have been demonstrated in adults with drug therapy used as an adjunct to lifestyle changes. However, the newer drugs have not been extensively studied in older adults. The long-term effects of lorcaserin, as well as combination phentermine and topiramate extended release on cardiovascular morbidity and mortality are unknown. Neither medication has been studied in patients using concomitant insulin. Older adults at high risk for cardiovascular morbidity and mortality who have tried lifestyle changes alone and were unable to achieve at least a 5% reduction in weight loss may benefit from behavioral therapy.

**Thyroid Disease**

Individuals with thyroid disease, including hypothyroidism, hyperthyroidism, and thyroiditis, comprise about 7.35% of the population.\textsuperscript{10} Thyroid diseases are common in older adults, especially women. Despite their frequency, thyroid diseases may be a challenge because their presentation may differ from that in young or middle-aged adults. The symptoms of hyperthyroidism and hypothyroidism in older adults are easily misinterpreted as part of the aging process and usually develop slowly over time. Clinicians should routinely consider thyroid diseases as a potential diagnosis in older adults. For example, a patient with new-onset atrial fibrillation due to a thyroid disorder has no symptoms from the arrhythmia, nor does the patient have...
other signs or symptoms of thyroid disease. In addition, thyroid function tests may be altered by nonthyroidal diseases in older adults. Finally, recent NHANES III data demonstrated that the 97.5th percentile of serum TSH increases by 0.3 milli-international units per liter every 10 years after age 39. This increase is independent of body weight, antithyroid antibody, and urinary iodine excretion.57

Etiology, Epidemiology, and Clinical Presentation in Older Adults

Hyperthyroidism

In the United States, the most common causes of hyperthyroidism are Graves’ disease, uni- or multinodular goiters, and toxic adenomas.61-63 An estimated 10% to 15% of patients over 60 have hyperthyroidism.61 Between 50% to 80% of patients with hyperthyroidism have Graves’ disease caused by thyroid-stimulating antibodies.62 The peak incidence of hyperthyroidism is in the second to fourth decade of life, although hyperthyroidism including Graves’ disease occurs in older adults as well. The prevalence of multinodular goiter and toxic nodules as a cause of hyperthyroidism is increased in older adults.64 Women are at higher risk of Graves’ disease than are men; however, older men have the highest risk of severe ophthalmopathy from Graves’ disease.63

Although some older adults will have the classic symptoms of hyperthyroidism, such as tremor, nervousness, increased appetite, heat intolerance, and diarrhea, many will lack these presenting complaints. Palpitations, angina, and especially atrial fibrillation with a slow ventricular response may be more common presenting cardiovascular symptoms in older adults.62,63 Muscle wasting, especially of the quadriceps muscle in the thigh, may be present and increases the risk of falling in older adults.64 One form of Graves’ disease, apathetic hyperthyroidism, is more common in older adults and may actually present with symptoms of apathy, weakness, lethargy, and severe depression, which can make the diagnosis of thyroid storm very difficult.65 One report identified the presence of apathy, tachycardia, or weight loss as strong predictors of thyrotoxicosis in older adults.65

Hypothyroidism

The incidence of hypothyroidism increases with advancing age and is more common in women than in men. An estimated 10% of women and 2% of men over 60 have hypothyroidism.61 Hypothyroidism is divided into primary (in which the thyroid gland is unable to respond to stimulation by thyroid-stimulating hormone [TSH]) or secondary (due to a pituitary or hypothalamic cause). The latter type is rare in older adults. Hypothyroidism in older adults is frequently due to autoimmune disease such as Hashimoto’s thyroiditis or chronic autoimmune thyroiditis.57,63,66 Hypothyroidism may also result from the treatment of Graves’ disease, especially following the use of radioactive iodine or thyroidectomy.67 TSH should be measured every 6–12 months in individuals treated with radioactive iodine as the risk for hypothyroidism after its use remains 2% to 3% per year after the first year. Drugs such as amiodarone, lithium, interferon, propylthiouracil, and methimazole may also cause hypothyroidism.

Many signs and symptoms of hypothyroidism are easily attributed to the aging process. Older adults may present less frequently with weight gain, cold intolerance, muscle cramps, and paresthesias than younger adults with hypothyroidism. Hypertension, hyperlipidemia, bradycardia, as well as both pitting and nonpitting edema may be attributed to comorbid diseases and drug therapies. Most importantly, neuropsychiatric symptoms, including depression and impaired cognition, may be present in older adults with hypothyroidism. A recent cohort study from the Framingham study indicated that women who had TSH concentrations <1.0 milli-international units per liter (lowest tertile) and over 2.1 milli-international units per liter (highest tertile) were at increased risk of Alzheimer disease.68
KEY POINT: A TSH concentration should be obtained to rule out potentially reversible causes of dementia in older adults.

Subclinical Hypothyroidism

Subclinical hypothyroidism is a common thyroid disorder with a prevalence of over 15% among older women. The serum TSH concentration is elevated, although the free thyroxine (T4) concentrations are within the normal range. Individuals may have antithyroid antibodies, suggesting an autoimmune basis for the condition. Patients may have a history of Graves’ disease and/or the prior use of lithium or an iodine-containing medication such as amiodarone. The likelihood of developing hypothyroidism may be 4% per year for women with positive antibodies and elevated TSH based on data from the Whickham survey. Screening for the development of clinical hypothyroidism is recommended every 5 years. In general, if the serum TSH concentration is >10 milli-units per liter, levothyroxine is initiated whether or not the patient is symptomatic. For individuals who are asymptomatic and who have serum TSH concentrations between 4 and 10 milliunits/L, monitoring is generally recommended. Although subclinical hypothyroidism may be treated based on symptoms and TSH concentrations, evidence is lacking to support an association between mild cognitive impairment and subclinical hypothyroidism in older adults.

KEY POINT: Initiation and dosage adjustment of levothyroxine should be made based on assessment of T4 and TSH, rather than TSH alone, to avoid inappropriate treatment.

Euthyroid Sick Syndrome

The euthyroid sick syndrome (ESS) has been described as abnormal thyroid function tests in patients with serious nonthyroidal diseases such as gastrointestinal, pulmonary, renal, or cardiovascular illnesses. These patients lack a prior history of hypothalamic, pituitary, or thyroid disease. In general, serum T3 concentrations are low and the reverse T3 uptake is elevated. Serum concentrations of T4 are usually in the normal range and TSH may be slightly decreased. In severe nonthyroidal illnesses such as sepsis, concentrations of T3, T4, and TSH may be reduced, with an elevated reverse T3 uptake. Patients with ESS often have elevated cortisol concentrations. After recovering from the illness, thyroid function tests return to baseline values. Whether the nonthyroidal disease is causing an artificial effect on the thyroid function tests or whether it reflects a true change in thyroid functioning is unknown. Although advancing age is not necessarily a risk factor for ESS, older adults have an increased prevalence due to the greater risk of having multiple chronic diseases. The primary treatment is focused on managing the underlying illness and monitoring thyroid function tests during and after recovery.

Summary of Standard Treatment

The recommended treatment for hyperthyroidism consists of the use of antithyroid drugs, radioactive iodine (I-131), or thyroidectomy. The antithyroid drugs, propylthiouracil and methimazole, inhibit thyroid peroxidase and the resulting synthesis of thyroid hormone. Propylthiouracil also inhibits the peripheral conversion of thyroxine (T4) to triiodothyronine (T3), so that symptoms may resolve more quickly. Methimazole has a longer half-life that permits once-daily dosing of the drug compared to propylthiouracil, which requires multiple daily doses. In a comparative study of once-daily methimazole and once-daily propylthiouracil, methimazole induced euthyroidism more quickly than propylthiouracil. Therapy with antithyroid drugs is continued for 6 to 18 months. The use of I-131 results in radiation-induced destruction of the thyroid gland, while thyroidectomy removes all or part of the thyroid gland. Adjunctive therapy includes beta-adrenergic blockers to control the tachycardia, tremor, and other symptoms of
adrenergic excess, or if contraindicated a nondihydropyridine calcium channel blocker such as verapamil. In addition, supersaturated potassium iodine and glucocorticoids can be used in preparation for thyroid surgery.63

The goals of treatment for hypothyroidism are to control symptoms and prevent myxedema, which is rare but occurs more commonly in patients older than 75 years. The recommended first-line treatment for hypothyroidism is levothyroxine. Although other preparations such as desiccated thyroid, triiodothyronine, and combination products containing T4 and T3 are available, these formulations do not offer clinical advantages over levothyroxine for most patients. Dessicated thyroid is an inappropriate drug to use in older adults because of its potential cardiac effects; this drug is on the list of Beers criteria drugs.72 A meta-analysis of 11 studies consisting of 1,216 patients evaluated the combination of T4 and T3 versus T4 monotherapy in clinical hypothyroidism. Bodily pain, quality of life, depression, fatigue, and anxiety were similar between the two treatments. In addition, cognitive functioning, lipids and lipoproteins, and adverse effects were similar. Based on this evidence, a combination product of T3 and T4 does not offer compelling advantages in clinical hypothyroidism.73

Treatment Recommendations for Older Adults

Hyperthyroidism

The treatment of hyperthyroidism in older adults usually involves the use of I-131 and antithyroid drugs. I-131 is preferred in older adults because the treatment is effective and the long-term risks are of less concern. In addition, if hyperthyroidism recurs (such as following the use of antithyroid drugs), older adults may have an increased risk of atrial fibrillation.63 Patients generally become euthyroid within 6–12 weeks after receiving I-131, and many individuals eventually become hypothyroid.64 The use of I-131 in older adults with underlying ischemic heart disease may increase the risk of radiation-induced thyroiditis due to the release of preformed thyroid hormone from the gland. To prevent this effect, antithyroid drugs may be administered for 1–2 months and then discontinued for 3–5 days before administering the I-131.71

Another approach to the treatment of hyperthyroidism is to use antithyroid drugs as the first-line treatment. Propylthiouracil is dosed 50–100 mg every 8 hours and methimazole 15–30 mg once daily. Antithyroid drugs are administered for 6–18 months, and thyroid function tests are monitored every 2 months at least early in therapy. Adverse effects include skin rashes, arthralgias, and myalgias. Although rare, agranulocytosis may be more common in older adults, primarily occurring in the first 90 days.74

Hypothyroidism

The treatment of hypothyroidism should begin with 12.5–25 mcg of levothyroxine daily, especially in older adults with underlying ischemic heart disease or heart failure.57 Although older adults may be less likely to absorb T4 as well as young individuals, they may require a smaller starting dose because of decreased lean body mass.57 Serum TSH concentrations should be monitored after 4–6 weeks and after any subsequent dosage adjustment.64 Dosage adjustments should be between 12.5 and 25 mcg, and symptoms should be carefully assessed. The goal is to have the TSH within the normal reference range and to prevent overreplacement, which might increase the risk of precipitating cardiac symptoms and of worsening osteopenia or osteoporosis.

Levothyroxine should be dosed once daily on an empty stomach. In addition to foods, such as fiber, decreasing the absorption of levothyroxine, many drugs and minerals may also prevent its absorption. Bile acid sequestrants such as colestipol and minerals such as calcium and iron may decrease levothyroxine absorption. Other drugs such as phenobarbital, phenytoin, carbamazepine, and rifampin may increase the hepatic metabolism of levothyroxine. A thorough medication history is essential for older adults taking levothyroxine.
Key Point: As patients become euthyroid after treatment of hyperthyroidism or hypothyroidism, their entire drug regimen should be carefully reviewed. The clearance of some medications may have been increased or decreased, and dosage adjustments may be indicated to maintain the safety and efficacy of the drug regimen.

Pituitary Gland Dysfunction

The pituitary gland is responsible for the secretion of hormones such as adrenocorticotropic hormone and growth hormone (GH). Although little data exist on the prevalence of pituitary gland disorders in older adults, GH deficiency may occur in some older adults. One study demonstrated that GH replacement can increase lean muscle mass, reduce adipose tissue, and increase markers for bone metabolism in older adults with pituitary disease. GH has been promoted extensively as an anti-aging therapy, although the evidence of its safety and efficacy in older adults is limited. A 26-week study of 131 healthy community-dwelling adults between 65 and 88 demonstrated increased lean body mass and decreased fat mass, while muscle strength was unchanged. The long-term safety of GH remains unknown; potential concerns include diabetes and glucose intolerance, peripheral edema, joint pain, carpal tunnel syndrome, gynecomastia, and potentially an increased risk of cancer.

Changes in Sex Hormones in Older Adults

Menopause

Most women will experience menopause between the ages of 45 and 55, as a normal part of aging. With this “change of life,” women may experience vasomotor symptoms such as hot flashes as well as vaginal atrophy and dryness. During this time, the risk of developing coronary heart disease (CHD), osteoporosis, breast and colorectal cancer, and cognitive impairment increase significantly.

Over the past 40 years, many observational studies and small clinical trials suggested that hormone therapy (HT) with either estrogen alone or in combination with a progestin had health benefits in older women. Although findings from observational studies were consistent, they were flawed. Women who were using HT in cohort studies were different from women who chose not to use hormones, in that they were healthier and more adherent. In addition, these women typically had begun using HT soon after menopause.

The findings of the Women’s Health Initiative (WHI) challenged traditional beliefs about the risks and benefits with HT. Over 162,000 postmenopausal women between the ages of 50 and 79 were enrolled in three clinical trials and an observational study. One clinical trial evaluated the risks and benefits of HT in 16,608 women without CHD. The active treatment included conjugated equine estrogens 0.625 mg plus medroxyprogesterone 2.5 mg daily in women who had an intact uterus. A second WHI study of 10,739 women used conjugated equine estrogens 0.625 mg daily in women who had undergone a hysterectomy. Nonfatal MI and death due to CHD were the primary outcome measures, and the development of invasive breast cancer was the primary adverse outcome. The outcomes are summarized in Table 10-3. A recent analysis indicated that most risks and benefits declined following discontinuation of HT, although the increased breast cancer risk continued during the follow-up period.

Attention has focused recently on the timing hypothesis, in which the benefits of HT may outweigh the risks when used either in the first 10 years after the onset of menopause or up to age 60. For example, with cardiovascular...
disease, the use of HT in older women may result in plaque destabilization if atherosclerosis is present, potentially resulting in stroke and MI. Similarly, benefits from HT on cognition and the risk of Alzheimer disease were apparent in observational studies, while the WHI substudy on memory demonstrated an increased risk of dementia among older women given HT.84 Use in older women must be carefully individualized, with specific recognition of the limited role of HT.82-84

**Andropause**

The term andropause has been used to describe a syndrome in some middle-aged and older men that includes decreased energy, impaired libido and erectile dysfunction, muscle weakness, and depression. Over the past 10 years, the use of different testosterone products has been extensively promoted to improve these symptoms. One report evaluating androgen prescribing between 2001 and 2011 demonstrated a threefold increase in their use in all age groups, including men 70 and older. Prescriptions for testosterone gel formulations increased fivefold during this time period. Although almost three-quarters of men taking these products had a testosterone level, the prevalence of low values is unknown.85

Similar to the use of HT in women before the findings of WHI were published, evidence supporting the safe and effective use of different testosterone products from randomized clinical trials has been limited. Low testosterone concentrations have been associated with obesity, diabetes, incident and severity of coronary artery disease, as well as cardiovascular and all-cause mortality in observational studies.86 Effects of testosterone replacement on lipids have been mixed, and a lowered total cholesterol reported in some studies. Although observational studies and some clinical trials have suggested other potential benefits, the clinical studies have enrolled small numbers of patients and were typically of short duration.86 However, in a randomized, placebo-controlled study of 209 men with a mean age of 74 years and limitations in mobility, daily use of a 1% testosterone gel resulted in improvements in leg press and chest press strength, as well as in climbing stairs.87 Although effective in raising testosterone concentrations, concerns have increased about testosterone’s cardiovascular safety. A retrospective cohort study used data from 8,709 men in the Veterans Affairs health system who had undergone coronary angiography. The men had testosterone concentrations below 300 ng/dL and 1,223 received a testosterone product. The primary outcome measure was a composite of MI, ischemic stroke, and all-cause mortality. Men receiving hormone therapy had an absolute increase in the risk of the primary outcome measure of 5.8% over men who were not receiving the drug therapy at 3 years after

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**Table 10-3. Selected Potential Risks and Benefits of Oral Hormone Therapy (Estrogen plus Progestin) in Older Women**

**Risks**

- Increased risk of thromboembolic disease in the first year.
- Increased risk of coronary heart disease and stroke within the first several years, highest among older postmenopausal women.
- Increased risk of breast cancer with longer duration, which rapidly decreases with cessation of therapy.
- Potentially increased risk of ovarian cancer.
- Potentially increased risk of dementia possibly due to silent small strokes, and no benefit in mild cognitive impairment.

**Benefits**

- Decreased risk of hip and related fractures.
- Decreased risk of invasive colorectal cancer, although it is diagnosed at a more advanced stage.
- Decreased moderate-to-severe vasomotor symptoms, although no overall benefit on health-related quality of life.
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coronary angiography. Another cohort study from a large healthcare database assessed the risk of nonfatal MI in men in the first 90 days after receiving their first prescription for testosterone therapy. The comparator group included men from the same database who received their first prescription for either sildenafil or tadalafil. The rate ratio for MI was 2.19 (95% CI 1.27, 3.77) for men over 65 that increased to 3.43 (95% CI 1.54, 7.66) for those men 75 and older. A similar trend was not reported with sildenafil and tadalafil. Based on the findings of these two studies and ongoing monitoring, the Food and Drug Administration has decided to reassess the safety of testosterone products.

**SEXUAL DYSFUNCTION**

Sexual intimacy and activity remain important even into late life. A nationally representative survey reported the prevalence of sexual activity among 3,005 community-dwelling older Americans between the ages of 57 and 85. Sexual activity was defined as a mutually voluntary activity with another person that involved sexual contact regardless of whether or not intercourse or orgasm occurred. Among respondents ages 57 to 64, the prevalence of sexual activity was 73%, while among those 65 to 74 years and 75 to 85 years the prevalence was 53% and 26%, respectively. Among sexually active adults between the ages of 75 and 85, 54% reported sexual activity at least two to three times per month and 23% indicated sex at least once a week. Although a lack of a partner or the presence of a partner with serious health-related issues may limit the frequency of sexual function, older adults, similar to younger individuals, value sexual activity as a part of maintaining close personal relationships.

**Etiology, Epidemiology, and Clinical Presentation in Older Adults**

Erectile problems are the most commonly reported sexual dysfunction, with an estimated prevalence of 37% of older men. The annual incidence of erectile dysfunction was 12.4 per 1,000 person-years among men 40–49, 29.8 among men 50–59, and 46.4 among men 60–69 years old. After adjusting for age, the risk of erectile dysfunction was higher among men with hypertension, diabetes, and heart disease.

Normal erectile functioning is the result of a complex interplay between endocrine, vascular, neurologic, and psychosocial factors. Erectile dysfunction, defined as the inability to attain or maintain an erection sufficient for satisfactory sexual intercourse, may be due to many factors. Vascular causes such as atherosclerosis from diabetes, as well as neurological problems following a stroke may result in erectile dysfunction. Many drugs may also contribute to it.

**KEY POINT:** Erectile dysfunction in older men is a multifactorial condition. Attention should be focused on optimal treatment of underlying diseases such as hypertension and diabetes, rather than considering it solely an adverse effect of drugs.

Sexual dysfunction in men may also include changes in libido, ejaculation, and orgasm, and commonly occurs with advancing age. Testosterone concentrations may decline by 1% to 2% per year, and levels of free testosterone decrease by up to 30% in men in their seventh decade of life. Luteinizing hormone is reported to be higher than among younger men.

Women have reported less sexual activity across all age groups compared to men. Among women ages 75–85, only 16.7% reported sex with a partner in the prior 12 months, while 38.5% of men had engaged in sexual activity. In a recent survey, decreased libido, difficulty with vaginal lubrication, and the inability to climax was reported by 43%, 39%, and 34%, respectively. Female sexual dysfunction has been classified as disorders of desire, arousal, orgasm, and sexual pain or dyspareunia. Sexual dysfunction among women may be caused
by many factors, including physiological and hormonal changes resulting from menopause as well as relationship, physical, and mental health problems. In addition, older women frequently may lack a partner or have a partner with serious health-related issues, which limits their sexual activity.

**Summary of Standard Treatment**

The first-line pharmacotherapy of erectile dysfunction in men consists of the oral phosphodiesterase type 5 (PDE-5) inhibitors including sildenafil, tadalafil, vardenafil, and avanafil. The transurethral or intracavernosal administration of alprostadil also enhances the smooth muscle relaxation needed to attain an erection. Testosterone therapy, especially in a transdermal formulation, is reserved for men with documented hypogonadism. Penile devices, including a vacuum pump and a surgically-implanted penile prosthesis, have been used in men who either do not respond or who have contraindications to drug therapy. Psychotherapy may be used when the erectile dysfunction is believed to have a psychogenic etiology.94

The treatment of sexual dysfunction in women depends on the underlying cause and the specific sexual disorder. For example, symptoms of vaginal dryness can be treated with topical lubricants. The treatment of hypoactive sexual desire disorder has included nonpharmacologic and educational approaches as well as drug therapy. Transdermal testosterone in a dosage of 300 mcg daily has been used, although not commercially available for arousal disorders. A 6-month study of 814 postmenopausal women ages 20 to 70 with hypoactive sexual desire disorder evaluated the effectiveness of 150-mcg and 300-mcg testosterone patches compared to a placebo patch. Although the higher dose patch demonstrated some benefit, the effects were modest.95

PDE-5 inhibitors have been studied for disorders in desire, arousal, and orgasm in women with inconsistent results. Sexual pain disorders have been treated with psychotherapy and other nonpharmacologic approaches. Dyspareunia due to vaginal atrophy has been managed primarily with oral and topical estrogens. Ospe-mifene, an oral estrogen agonist/antagonist, was recently approved for the treatment of moderate to severe dyspareunia.

**Treatment Recommendations for Older Adults**

The treatment of sexual dysfunction in older men and women involves first identifying and appropriately managing the potentially contributing factors. Many diseases and drugs may adversely affect sexual functioning; however, the cause of sexual dysfunction is frequently due to multiple factors.

Contraindications to the use of PDE-5 inhibitors may be more likely to be present in older men due to the presence of underlying cardiovascular disease. Although generally safe, their use in older men raises several potential concerns. All PDE-5 inhibitors are contraindicated in individuals taking nitrates because of the risk of severe hypotension, as vasodilation from the anti-ischemic therapy may be significantly increased because both drugs are nitric oxide donors.96 In general, nitrates should be avoided for at least 24 and 48 hours following the use of sildenafil (and vardenafil) and tadalafil, respectively.

Older men should also be carefully evaluated with regard to underlying coronary artery disease (CAD) because of concern that increased sexual activity theoretically might increase the risk of coronary ischemia. Patients who are considered to be at intermediate risk include those who have CAD and at least three other risk factors, such as a recent MI or stroke. Individuals at high risk include those men with unstable angina and uncontrolled risk factors such as class III or IV heart failure or an MI in the past 2 weeks.97
Older men with documented hypogonadism as the cause of their erectile dysfunction may be candidates for testosterone therapy, although the testosterone concentration should be <200–300 ng/mL. Multiple testosterone products are available, including depot injectable formulations, patches, gels, and buccal tablets. Testosterone enanthate or cypionate is started at a dosage of 75–100 mg intramuscularly weekly or 150–200 mg every 2 weeks. Testosterone patches may be started at one to two 5-mg patches applied to the back, neck, or upper arm every night. The testosterone gel (Androgel, Testim) is applied in the morning to clean, dry nonscrotal skin in a starting dosage of 5 g, which delivers 5 mg of testosterone daily. A self-adherent buccal tablet of 30 mg of testosterone is also available and dosed twice daily. The tablet is placed between the inner cheek and the gums above the incisor tooth and held firmly in place for 30 seconds using a finger. The rounded side of the tablet should be against the gums. The tablet remains in place until the epithelial cells are shed in 12–15 hours. The dosage of these testosterone products is increased based on the serum testosterone concentrations obtained 2–3 months after starting the products.

In addition to the previously discussed cardiovascular concerns, adverse effects include the development of polycythemia vera; therapy should be stopped if the hematocrit exceeds 55%. Sleep apnea may worsen if risk factors such as obesity and chronic lung disease are present. Gynecomastia may also occur with testosterone therapy. Older men receiving testosterone should be carefully monitored for worsening benign prostatic hyperplasia (if present). The prostate specific antigen concentrations should also be carefully monitored and a digital rectal exam performed at least yearly.

Other monitoring of testosterone therapy is product specific. In men receiving the buccal formulation, potential changes in taste and irritation of oral mucosa should be evaluated. For the injectable products, men should be asked about any fluctuations in mood and libido in the interval between injections. The development of skin irritation should be carefully monitored with the use of testosterone patches. Although testosterone gels may also cause skin irritation, the most important education issue is to ensure that the skin-to-skin transmission of the testosterone to women and children is avoided to minimize potential exposure to the hormone.

Sexual dysfunction in women is also multifactorial, and concomitant drug therapy such as selective serotonin reuptake inhibitors (SSRIs) and aromatase inhibitors potentially contribute to symptoms. A woman may present with symptoms of painful intercourse or dyspareunia, decreased sexual desire, reduced arousal, or orgasmic dysfunction. The appropriate treatment depends on the presenting symptoms. For dyspareunia due to vulvovaginal atrophy, a nonprescription vaginal lubricant or long-acting moisturizer can be tried initially. Vaginal lubricants can be classified as water-based, silicone-based, or oil-based. In general, iso-osmolar water-based products, as well as silicone-based products, are preferred, although comparative studies in older women are not available. Vaginal, transdermal, and oral estrogens are also options. Vaginal estrogen products include creams, rings, and tablets and are effective without disrupting vaginal flora. Ospemifene is a newly approved selective estrogen receptor modulator (SERM) that is an oral treatment for moderate to severe dyspareunia. Similar to other SERMs, the drug may increase menopausal symptoms such as hot flashes, and the risk of uterine cancer and venous thromboembolism is unclear. The use of drug therapies such as testosterone and other androgens for
reduced sexual desire and PDE-5 inhibitors for decreased sexual arousal and orgasm in older women remain controversial and are not generally recommended. For the woman who has developed sexual dysfunction from an SSRI, a switch to bupropion may relieve her symptoms if contraindications to the latter antidepressant do not exist. Finally, both older men and women should be counseled to avoid use of natural products for sexual functioning, especially products bought online, without first discussing their potential use with a healthcare provider.
**CASE 1: DIABETES MELLITUS**

**Setting:**
Outpatient geriatric clinic.

**Subjective:**
LR is an 84-year-old man who presents for follow-up with his primary care physician after an emergency department visit for elevated blood pressure.

**Past Medical History:**
Hypertension x18 years, diabetes mellitus type 2, GERD, osteoarthritis (OA), anxiety, history of pneumonia, history of falls.

**Medications:**
Lisinopril 20 mg once daily, amlodipine 5 mg once daily, aspirin 81 mg once daily, Lantus 30 units subcutaneously every morning, omeprazole 20 mg once daily, acetaminophen 325 mg 1–2 tablets every 6 hours as needed, tramadol 50 mg every 6 hours as needed, zolpidem 5 mg at bedtime, One Touch Ultra test strips 3–4 times daily and when sick.

**Allergies:**
Ibuprofen (upset stomach), penicillin (rash).

**Family History:**
Father passed away at age 75 and had type 2 diabetes, mother passed away at age 81, brother is alive and also has type 2 diabetes.

**Social History:**
Denies use of tobacco or alcohol. Does not exercise consistently but goes for a walk every now and then “when the weather is nice,” using a walker to ambulate. Lives in an assisted living facility and has Medicare Part D.

**Objective:**
Ht 61˝, Wt 125 lb, BP 154/92 BPM, HR 72. Recent blood glucose readings (11 a.m.): 161, 110. HbA1c today: 7.8%. Serum creatinine: 0.9 mg/dL. GDS score 3/15 (3 months ago), 6/15 (today).

**Assessment:**
LR is an 84-year-old man with type 2 diabetes, uncontrolled blood pressure, and possible depression. He is at risk for future falls.

**Plan:**
1. An appropriate target HbA1c for LR is <8 %, given his age and risk for falls due to medications, pain, and use of walker. His HbA1c can be checked every 12 months, or sooner if changes are made to his Lantus. It would be reasonable to reduce his blood glucose monitoring to once daily in the morning and when he is sick.
2. Discuss with LR whether he has been adherent with his lisinopril and whether or not he is able to afford his medications in order to take them consistently. A dosage increase would be appropriate if he is adherent. Assess his diet for sources of sodium. Monitor his blood pressure and target <140/90 mmHg, although a higher systolic BP may be acceptable (<150).
3. Review LR’s responses on the Geriatric Depression Scale and discuss any precipitating events that may have increased his score. Assess whether the depression may be short-term or related to his chronic disease, and whether he may benefit from a trial of medication.
4. LR should be assessed for ability to transfer on his own with and without a walker. LR should engage in moderate-intensity aerobic and resistance exercises to build strength.

**Rationale:**
A less stringent target HbA₁₀₀ may be appropriate for older adults with poor health, frailty, multiple comorbidities, or risk of falls. Self-monitoring of blood glucose should be individualized for older adults based on benefit, cost, and convenience. Older adults with type 2 diabetes should be screened for depression at the time of diagnosis and if a decline in function is observed. Moderate-intensity exercise has been shown to increase strength, decrease the loss of lean body mass, and improve cardiorespiratory function.

**Case Summary:**
This case illustrates the appropriate goals for an older adult with controlled type 2 diabetes and uncontrolled hypertension. It also highlights the potential for depression in older adults with type 2 diabetes and the benefits of regular exercise.
**Case 2: Hypothyroidism**

**Setting:**
Family medicine clinic.

**Subjective:**
ST is an 81-year-old woman presenting to the family medicine clinic for review of her medications and for annual influenza vaccination. She reports that she missed just one or two doses of medication in the past month. She denies any adverse effects from her medications. She mentions that she has been feeling more tired than usual and is having a little difficulty participating in activities because of this. She has also been eating more sweets recently.

**Past Medical History:**
Hypertension, osteoporosis, mild cognitive impairment, obesity, GERD, and dry eyes.

**Medications:**
Hydrochlorothiazide 25 mg once daily, calcium/vitamin D 600 mg/400 International Units twice daily, omeprazole 20 mg once daily, multivitamin once daily, docusate twice daily, acetaminophen as needed.

**Allergies:**
Morphine (nausea).

**Family History:**
Noncontributory.

**Social History:**
Quit smoking 50 years ago, has a few glasses of wine during the holidays, lives by herself in the community.

**Objective:**
Ht 61˝, Wt 184 lb, BP 142/90 BPM, HR 76, T4 within normal range, TSH 5.8 milliunits/L, MMSE 24.

**Assessment:**
ST is an 81-year-old woman with possible subclinical hypothyroidism and obesity. Potential symptoms of hypothyroidism include fatigue and constipation.

**Plan:**
- Assess ST’s current diet and activity level to determine whether her symptoms may be relieved through lifestyle interventions. If ST’s condition does not improve, re-evaluate TSH and compare to usual levels to determine whether or not her level has increased significantly. If a diagnosis of subclinical hypothyroidism is made, levothyroxine 12.5–25 mcg once daily in the morning would be appropriate.
- Counsel ST regarding the overall health benefits of exercise. If her weight does not decrease after adjustments are made to her levothyroxine, her TSH becomes stable, and weight loss is still desired, consider dietary counseling and energy restriction if nutritionally appropriate.
- Counsel ST regarding potential for drug interaction if calcium is taken within 4 hours of levothyroxine.
- Complaints of constipation can be addressed with symptomatic interventions such as laxatives on a short-term, as-needed basis, with or without the stool softener she already
receives. Anticipate that constipation will improve with correction of hypothyroidism and physical activity, rendering a long-term bowel regimen unnecessary. An evaluation of constipation would be recommended if symptoms do not resolve.

Rationale:
The reference interval for TSH may increase with age. However, older adults do not always exhibit classic symptoms of hypothyroidism, so follow-up will be necessary to determine whether ST’s complaints are due to hypothyroidism rather than poor diet and low energy expenditure. Her T4 is within normal range, suggesting subclinical hypothyroidism if thyroid disorder is present. Exercise may improve strength, emotional health, constipation, and pain and discomfort due to chronic illnesses.

Case Summary:
Subclinical hypothyroidism may be more difficult to diagnose in the elderly. If treatment is needed, levothyroxine is the best first-line choice and should be started at low dosages. Obesity may worsen the symptoms of hypothyroidism, and individuals with a BMI of 30–<35 kg/m² should be encouraged to pursue weight loss through changes in diet and physical activity.
Clinical Pearls

- Older adults taking antipsychotic medications should be closely monitored for signs and symptoms of hyperglycemia. The risk of developing new-onset diabetes from antipsychotic medications appears to be inversely related to age. However, glucose dysregulation may be problematic among older users of antipsychotics with pre-existing diabetes.

- Assessment of blood glucose can be difficult for an individual with cognitive impairment who resists fingerstick testing. If monitoring activities routinely turn into a battle resulting in acute agitation, caregivers may find themselves facing tough choices regarding whether to monitor less frequently, reduce or withdraw drug therapy, turn to psychoactive drug therapy, or employ alternate testing methods such as urine dipstick. The risk-benefit and the rationale for the strategy employed should be carefully documented.

Chapter Summary

Endocrine diseases such as diabetes mellitus, hypothyroidism, and obesity are common among older adults. Although they can be safely and effectively treated with standard approaches such as drug therapy, attention must be focused on establishing appropriate goals for the individual patient that take into consideration factors such as life expectancy and level of frailty, comorbid conditions, and concomitant drug therapy. The old aphorism of “start low and go slow” remains particularly applicable to the management of endocrine disorders in older adults.

Self-Assessment Questions

1. What are the advantages and disadvantages of the available drug therapy to manage diabetes mellitus in older adults?

2. What are common risk factors, presenting symptoms, and management approaches for hypoglycemia due to drug therapy in older adults with diabetes?

3. What are common risk factors, presenting symptoms, and management approaches for HHNS?

4. Describe the available pharmacologic and nonpharmacologic interventions used for weight loss and determine which have evidence of benefit in older adults.

5. Compare and contrast hypothyroidism, subclinical hypothyroidism, and ESS in terms of underlying etiology, presentation, laboratory tests, and management.

6. What are the advantages and disadvantages of the three primary treatments of hyperthyroidism in older adults?

7. How do the available oral medications for hypothyroidism differ?

8. What are the primary risks with the use of PDE-5 inhibitors and testosterone products in older men?

9. What are the primary types of female sexual dysfunction and the potential treatments?

References


GASTROINTESTINAL DISORDERS AND NUTRITION

LISA C. HUTCHISON and REBECCA B. SLEEPER

LEARNING OBJECTIVES

1. Compare the prevalence of gastrointestinal (GI) disorders among different subgroups of elderly patients and young adults.

2. Assess the applicability of general adult treatment guidelines and management strategies for GI disorders to different age strata of elderly patients.

3. Recommend treatment goals and appropriate drug therapy for GI disorders in elderly patients.

4. Recommend treatment goals and strategies for maintaining optimal oral health and nutrition in elderly patients.

KEY TERMS AND DEFINITIONS

ASPIRATION: The drawing of food or liquid into the lungs with the respiratory current.

DYSGEUSIA: Altered taste sensation.

Fecal Impaction: A large lump of dry, hard stool that remains stuck in the rectum.

Laxative Abuse: Overuse of laxatives because of an eating disorder or in an attempt to have one or more soft bowel movements every day.

Megacolon: Abnormal dilation of the colon with diminished or absent peristalsis.

Oropharyngeal Dysphagia: Difficulty initiating or coordinating swallowing.

Sarcopenia: Loss of muscle mass and strength associated with aging but not associated with a specific inflammatory disease.

Xerostomia: Dry mouth.
**Introduction**

Gastrointestinal (GI) disorders are a common cause of discomfort and distress throughout the lifespan and significantly affect appetite, enjoyment of food, and nutrition. GI symptoms influence, and are influenced by, activity level, and as such are closely related to functional level and quality of life. Aging is associated with physiologic changes throughout the GI tract, resulting in increased incidence of dysphagia, gastroesophageal reflux disease (GERD), nausea, vomiting, diverticulitis, constipation, diarrhea, and malnutrition.

There are three primary challenges for the pharmacist caring for an individual with GI complaints. The first is to avoid or minimize GI symptoms caused or exacerbated by medications. The second is to optimally employ drug therapy as the intervention for various GI conditions. This can present a particular challenge, as there are consequences associated with the long-term use of most medications indicated to treat GI symptoms. Therefore, the clinician’s charge is often less about selecting the right medication to treat the symptoms than about the monitoring and ongoing evaluation of drug therapy utility. The third challenge, an overarching one, is to ensure the maintenance of optimal overall nutritional status. This chapter discusses the etiology, epidemiology, and clinical presentation of various GI disorders commonly seen in the aging population, summarizes standard treatment strategies, and discusses special considerations for older patients, including special considerations for specific subgroups of patients.

**Oral Health and Dysphagia**

**Etiology, Epidemiology, and Clinical Presentation**

A review of the GI system begins with an assessment of oral health. Oral health is associated with systemic health and nutritional status. A significant focus of a discussion of oral health is dental health and oral hygiene, but other considerations such as dry mouth, taste perversions, and vulnerability to thrush should not be overlooked.

Advancing age is correlated with decline in dental status, with the greatest decline observed in populations aged 75 years or older. Compared with younger cohorts, older adults have worse oral hygiene, poorer oral functional capacity, and a higher rate of gingivitis, dental caries, and tooth loss. Disability is also associated with poor oral health.

One of the most common oral health problems in older populations is denture stomatitis: oral lesions caused by ill-fitting dentures or poor denture hygiene and maintenance. Besides discomfort, inability to comfortably wear dentures can result in problems with nutrition and communication.

Microorganisms found in the oral cavity are associated with dental caries and also systemic disease. These include cardiovascular problems such as infective endocarditis, orthopedic problems such as prosthetic joint infections, and respiratory complications such as aspiration pneumonia. The risk of aspiration pneumonia increases when poor oral health is compounded by dysphagia.

Dry mouth, or xerostomia, is a common problem reported among older patients. It is a symptom that can be caused by a variety of systemic conditions, with Sjögren’s syndrome being particularly common, but a significant cause of dry mouth is medication related. In various studies, 17% to 32% of community individuals reported feeling dry mouth. The prevalence increased with age and was higher among women than men, and higher among individuals receiving medications than those who were unmedicated. When associated with drug therapy, this is reported as an adverse effect in 12% to 39% of noninstitutionalized older persons. Medications most likely to be associated with dry mouth include those with anticholinergic activity, such as tricyclic antidepressants, antihistamines, muscle relaxants, and bladder antispasmodics. In addition, diuretics, cloni-
dine, beta blockers, calcium-channel blockers, inhaled medications, and cytotoxic medications can be causes.14-17

**KEY POINT:** Drug regimen review may identify modifiable causes of dry mouth.

Although altered taste, or dysgeusia, can be associated with many conditions, such as renal failure, psychiatric disorders, hypothyroidism, neoplastic conditions, nasal disorders, dry mouth, gingivitis, and zinc deficiency, the most common cause of altered taste perception is drug therapy.18-24 The incidence varies by drug, but common medications that can cause taste perversions include (at therapeutic doses) inhaled corticosteroids or bronchodilators, nasal drainage of intranasal and ophthalmic medications, clarithromycin, lithium, divalproex sodium, amiodarone, omeprazole, interferon alfa, tobacco, and some chemotherapy agents.24-26 Dysgeusia can also be a sign of toxicity from digitalis, dextromethorphan, amphetamine, and buspirone.

Similarly, oral thrush is a problem that can be caused by many conditions, including immune deficiencies, cancer, thyroid disorders, uncontrolled diabetes, poor denture hygiene, and dry mouth, but a common cause is improper administration of inhaled corticosteroids.25-28

The combination of suboptimal oral hygiene, comorbid medical conditions, and medication use all contribute to multiple symptoms affecting the health of teeth, gums, and oral mucosa.

**Standard Treatment and Management Strategies in the General Adult Population**

In addition to regular brushing and flossing, regular dental check-ups are recommended every 6 months to provide cleaning and to evaluate the health of the teeth, gums, and oral mucosa. One of the best resources for general oral health recommendations for the adult popu-

**Evidence Base Supporting Treatment Recommendations in Elderly Patients**

The evaluation of the evidence base for the elderly requires identification of various subgroups.
The American Heart Association does not have different recommendations for dental procedure prophylaxis for elderly patients; rather, the considerations are based on medical history and risk factors. Therefore, the relevant subgroup considerations may more likely be individuals with and without dentures, and individuals with and without cognitive impairment. Another factor that should be routinely considered when a dental visit is scheduled is the presence of anticoagulants on the medication regimen. Although bleeding risk associated with invasive dental procedures often prompts the suspension of warfarin or other anticoagulant or antiplatelet therapy before the appointment, there is concern that the risk of thromboembolic events associated with subtherapeutic anticoagulation may outweigh the perceived bleeding risk in some cases. Consensus guidelines recommend that for individuals with a stable international normalized ratio (INR; defined in this case as >2 but <4), the risk of bleeding associated with outpatient dental procedures, including tooth extraction, is very small and that anticoagulant therapy should not be suspended. In addition, in most cases a single dose of antibiotics for prophylaxis does not warrant adjustment of anticoagulation regimen. Rather, an INR evaluation is recommended 72 hours prior to the procedure. Individuals receiving antibiotics, especially more than one dose, should also undergo a follow-up INR evaluation 2–3 days after initiating the antibiotic. Finally, these individuals should not receive orders for COX-2 inhibitors or nonsteroidal anti-inflammatory drugs (NSAIDs) for dental pain associated with the procedure.

Oral care for dentures is different than regular brushing and flossing of natural teeth. Like natural teeth, dentures should be brushed daily; however, harsh toothpastes (especially whitening products) should be avoided, and the dentures should also be removed and cleaned regularly with a cleaning solution. Although mild soap and water can be used, products that bear the ADA seal of acceptance have been evaluated for their effectiveness, safety to the individual, and safety for the denture materials. Dentures should be removed and rinsed under water after eating, and it is recommended to rinse or gently brush the inside of the mouth as well. When dentures are not being worn, they should also be kept moist to avoid drying and warping. Dentures can be placed in water or a soaking solution; the dentist providing the dentures can recommend the best solution, as this may depend on the materials used in their formulation. After soaking overnight, the dentures should be rinsed again before putting them back in the mouth. For denture wearers at risk for or experiencing oral thrush, additional care must be taken not to reintroduce organisms into the mouth via the dentures, which must be thoroughly cleaned. Mouth rinsing after administration of inhaled corticosteroids may need to be more stringent for denture wearers, with some data suggesting that rinsing three times may be necessary to sufficiently remove residual medication from mouth surfaces.

Oral care for an individual with functional or cognitive impairment can be especially challenging. Geriatric “sensitivity exercises” often require pairs of learners to give and receive oral care, often while blindfolded or physically restrained in other ways. It is a physically awkward maneuver, especially when the caregiver cannot perceive the degree of pressure of the brush on the surfaces of the mouth. The exercise illustrates the difficulty of achieving optimal cleansing while avoiding discomfort, even when the care recipient is actively participating and cooperating with the experience. This need for caution increases the risk of suboptimal oral cleansing; therefore, some studies suggest that in addition to brushing, wiping oral mucosa with a brush soaked in chlorhexidine can help improve malodor and reduce the risk of opportunistic infections.

**KEY POINT:** Warfarin therapy is often not optimally managed before or after dental procedures, resulting in unnecessary subtherapeutic anticoagulation.

Oral care for an individual with functional or cognitive impairment can be especially challenging. Geriatric “sensitivity exercises” often require pairs of learners to give and receive oral care, often while blindfolded or physically restrained in other ways. It is a physically awkward maneuver, especially when the caregiver cannot perceive the degree of pressure of the brush on the surfaces of the mouth. The exercise illustrates the difficulty of achieving optimal cleansing while avoiding discomfort, even when the care recipient is actively participating and cooperating with the experience. This need for caution increases the risk of suboptimal oral cleansing; therefore, some studies suggest that in addition to brushing, wiping oral mucosa with a brush soaked in chlorhexidine can help improve malodor and reduce the risk of opportunistic infections.
Regardless of which product is used, there is no single strategy that is effective for providing dental hygiene for all individuals with dementia. When dementia affects the individual’s cognitive perception, a caregiver’s attempts to assist with personal hygiene can be interpreted as confusing or threatening, and it can be difficult to achieve cooperation. Many different techniques have been evaluated in the literature, including eye level approach, verbal cueing, avoiding physical restraints, avoiding baby talk, and experimenting with various techniques such as face to face care versus “mirror-mirror” care (standing behind the individual). Supplementing brushing with rinses and oral swabs can help, but the patient must understand how to swish and spit rather than swallow, which often requires creative strategies tailored to the personality and preferences of the patient. Providing oral care to someone with cognitive or functional dependence is a significant challenge, but one worth addressing, as oral health interventions are associated with a reduction in the risk of a range of adverse outcomes, including aspiration pneumonia.

Special Considerations Affecting Desired Clinical Outcomes

Financial status is a significant barrier to optimal oral health in older patients. Although one study in the primary care setting demonstrated that the inclusion of a dental health check as part of a preventive care program was a feasible and effective way to increase dental visits among a population age 75 or older, elderly patients may experience barriers to paying for dental care. In most cases, Medicare does not cover routine dental work, and although Medicaid reimbursement rates can vary from state to state, low reimbursement rates may discourage some dental practices from accepting Medicaid beneficiaries as patients. For residents of long-term care facilities, particularly those with dementia, visits by dental health professionals may not be ideal. Given the association of poor oral health with systemic disease, this disparity can significantly influence healthcare outcomes.

Dysphagia

Etiology, Epidemiology, and Clinical Presentation

Dysphagia generally means difficulty swallowing but is actually defined in more than one way. Oropharyngeal dysphagia (OD), for instance, is difficulty initiating swallowing or coordinating the movement of food or liquid from the mouth to the upper esophagus. Esophageal dysphagia (ED) is difficulty transporting the food or liquid through the esophagus into the stomach. OD is the more common form in older adults. The prevalence of dysphagia in those age >65 years is not exactly known but estimated to be between 10% to 30%. However, the prevalence varies by subgroup, and comparing community-dwelling populations to long-term care populations, the prevalence is suggested to be higher, up to 50% in the institutionalized setting. In the hospital setting, dysphagia is associated with longer inpatient stays, higher incidence of complications, increased need for rehabilitation services, and increased need for post-discharge care in skilled units or long-term care facilities.

The most common cause of OD is neurological, associated with conditions such as stroke or Parkinson disease, and swallowing can also be affected by drugs such as antipsychotics, barbiturates, anticholinergics, diuretics, and mucosal anesthetics. Dysphagia occurring after stroke is reversible or improvable in a majority of cases; however, dysphagia associated with dementia or Parkinson disease has a poorer prognosis. Drug-induced esophageal injury such as ulcerations or strictures can also result in ED. Although there are some classes of medications, such as NSAIDs or bisphosphonates, for which the risk of esophageal injury is more understood, almost any medication could cause injury if administered improperly. Failure to administer medication with an adequate amount of water is a common oversight and can result in caustic injury or esophageal obstruction. Although the likelihood of a drug causing a caustic injury to the esophagus can be related to pH or dissolu-
tion properties, this can be also problematic for bulk-forming laxatives such as methylcellulose or polycarbophil.\textsuperscript{59,60} In addition, case reports of local adverse effects have been reported for a number of medications associated with dry swallowing or inadequate water.\textsuperscript{56,59,60}

\textbf{KEY POINT:} Administration of medications with adequate water is important but often overlooked and should be reassessed in the presence of GI symptoms.

The three most significant consequences of dysphagia are choking risk, aspiration pneumonia, and malnutrition.\textsuperscript{51-53,61,62} A decrease in ability to forcefully cough due to loss of pharyngeal support or compromised reflexes for coughing, gagging, or swallowing may occur because of age-related changes in the pharynx as well as decreased central nervous system (CNS) reflex activity.\textsuperscript{49,50} Coupled with reductions in the activity of ciliary transport and age-related changes in immune responsiveness, individuals with dysphagia are at increased risk for aspiration pneumonia.\textsuperscript{52,62} This is the most common cause of death in patients with dysphagia and is estimated to occur in 5\% to 15\% of cases recorded as community-acquired pneumonia.\textsuperscript{52,62} Difficulty swallowing food or liquid also compromises nutrition. Even when the consistency of food or liquid is altered to facilitate swallowing, the palatability of the altered diet often presents an obstacle to ensuring good nutrition and is a major factor affecting quality of life.\textsuperscript{63}

Although there are some common signs and symptoms that suggest dysphagia based on patient report, the health professional must be able to recognize nonverbal cues that suggest swallowing difficulty as well.\textsuperscript{64-66} Common complaints can include the sensation of food sticking in the throat, discomfort or pain on swallowing, coughing, or choking. Patients may also experience dyspnea, runny nose, watery eyes, nasal or oral regurgitation, and a “wet” vocal quality.\textsuperscript{64-66} Some signs of aspiration are silent but can be observed on x-ray as lung crepitation and consolidation. In the presence of unexplained fever or low oxygen saturation, aspiration pneumonia is one of the respiratory conditions that should be on the differential diagnosis list.\textsuperscript{52,62}

\textbf{Standard Treatment and Management Strategies in the General Adult Population}

The assessment and management of dysphagia is truly an inter-professional endeavor. Optimal, the assessment of swallowing function is performed by a speech therapist or speech language pathologist (SLP), but the referral for this service can be prompted by observations by a variety of health professionals or caregivers who recognize the signs of dysphagia or possible aspiration. There are two basic types of swallow evaluations: the Clinical Swallow Evaluation and the Videofluoroscopic Swallow Study. The clinical study is done at the bedside. The basic assessment of dysphagia begins with an evaluation of the individual’s level of consciousness, posture, voluntary cough, voice quality, and saliva control.\textsuperscript{64-66} The SLP will evaluate the strength, movement, and coordination of the muscles in the mouth and throat and will observe the individual’s ability to swallow saliva, food, and liquid. Alternatively, a diagnostic procedure referred to as a modified barium swallow employs continuous images, either through x-rays or a fiberoptic endoscope, to view barium as it passes through the pharynx, esophagus, and stomach. This method can detect whether barium enters the respiratory tract and provide data about how the pharyngeal and esophageal muscles are functioning.\textsuperscript{65,66}

There are a variety of different management strategies that can be recommended based on the type and severity of the swallowing problem identified. For some individuals, exercises to strengthen the muscles of the mouth or throat, or the use of maneuvers to better coordinate the movement of food or liquid through the chewing and swallowing process, are recommended.\textsuperscript{67-70} These can also have a favorable effect on vocal quality.\textsuperscript{71} However, one of the most common
Interventions is to alter the texture or consistency of the food or liquid. A mechanically altered diet consists of finely cut or chopped solids that are easier to chew and introduce no large solid pieces into the mouth. Alternatively, a puree diet alters the texture of the food item into a soft form that does not require chewing. For liquids, a cornstarch-based thickener can be added to achieve a nectar or honey consistency. Providing nutrition via a tube is controversial and will be discussed later.

From the point of view of the pharmacist, one of the most important considerations for the individual with dysphagia is how to ingest oral medication. When the ability to swallow medications is compromised, the choices are crushing oral dosage forms, selecting a liquid formulation, or selecting an alternate route of drug delivery (e.g., transdermal, intramuscular). Oral administration is preferable based on the understanding of age-related changes in pharmacokinetics (see Chapter 3).

Absorption and bioavailability of most medications will remain relatively efficient in the GI tract, as opposed to alternative routes that may be more compromised by age-related changes in skin and subcutaneous tissues. Oral dosage forms are often less expensive than transdermal or intramuscular. Among oral formulations, crushing or opening tablets or capsules may be preferred over liquid because liquid formulations tend to be more costly and the volume of liquid and the nature of the vehicle must be considered. Products formulated primarily for children will require higher volumes to achieve an adult dose. For medications formulated for adults, the volume necessary may be relatively small (e.g., 5–10 mL) for any one medication. Again, the overall volume of liquid could ultimately be large if multiple doses of multiple medications must be consumed. This can be especially problematic with elixir formulations that contain alcohol in the vehicle or in suspensions that use sorbitol. A small amount in a single dose might be negligible, but as the volume or number of doses increases, these can cause drug-alcohol interactions or cause or exacerbate significant diarrhea. If an oral dosage form can be crushed, this can be avoided. However, crushing or opening tablets or capsules may be unacceptable for some medications, such as formulations that are enteric-coated, extended- or controlled-release or medications that are direct irritants or whose bioavailability or safety profile is altered if the dosage form is compromised. In these cases, replacing products with an immediate-release version (ensuring appropriate dosing interval based on product) is necessary, or liquid, transdermal, or injectable forms must be considered.

**KEY POINT:** A report of dysphagia by the SLP or the presence of chart orders for altered diet or liquid consistency should prompt the pharmacist to evaluate the patient’s ability to swallow medications.

If aspiration pneumonia is suspected, the infection is likely to be polymicrobial. In general, anaerobes and *Streptococcus* spp. are the primary suspects; however, some researchers have questioned the empiric value of selecting antimicrobial therapy based on these assumptions alone. In fact, one investigation determined that lack of anaerobic coverage in the drug therapy regimens for elderly patients with aspiration pneumonia was not associated with a poorer outcome, even though anaerobic organisms had been identified via culture. New ideas suggest that relevant variables to consider may be the individual’s functional status (activities of daily living score), the presence of chronic underlying respiratory conditions, and whether an enteral feeding tube is present. These variables may suggest a higher prevalence of anaerobic to aerobic organisms, *Enterobacteriaceae, Pseudomonas aeruginosa,* and drug-resistant organisms, allowing more aggressive therapy to be directed at these targets for patients with such risk factors.
**Evidence Base Supporting Treatment Recommendations in Elderly Patients**

There are no specific differences in the approach to dysphagia based simply on age; however, there are some subgroups to consider when designing a treatment strategy, such as individuals with cognitive and functional impairments or those with a nasogastric or percutaneous endoscopic gastrostomy tube. Although a variety of interventions for safe eating and drinking can be recommended by the SLP, the ability to adhere to recommendations is influenced by cognitive and functional dependence. Adherence rates in the literature range widely, from 0% to 80%. It should not be a surprise that adherence to altered diet recommendations is challenging. The enjoyment of food and drink is such a fundamental part of quality of life that restrictions create dissatisfaction and resistance. It is an unhappy situation for everyone when what is safe is at odds with what is desired, and all individuals in this position will have to make a personal choice regarding how to prioritize and adhere to safe swallowing recommendations for long-term risk management. Sometimes, the choice will be nonadherence. Unfortunately, the individual’s motivation or ability to adhere is often overestimated, which may result in a lack of awareness of what the eating and drinking behaviors of the patient really are (privately or at the hands of caregivers). For instance, in one review of the literature, data describing compliance with safe swallowing techniques suggested SLPs estimated patient compliance to be 71.9%; however, the average compliance rate among the patient group was actually only 35.6%. The authors observed that patients were taught safe swallowing technique until they could successfully demonstrate performing the technique. But in many cases the intervention was not long enough to ensure understanding, and there was often poor patient motivation to continue. The authors suggested one of the keys to successful adherence was training and supervision. Data describing the impact of a training program for hospital staff found that the initial compliance rate was 51.9% for recommendations for fluid and diet consistency, amount of food given, physical strategies employed, and supervision. The most common caregiver reasons for noncompliance were inappropriate techniques and consistencies for thickened liquids by staff, lack of awareness of SLP recommendations, and inadequate patient supervision. The authors saw improvements with training but found that repeated training on a regular basis was needed because of high rates of staff turnover.

Pharmacists need to be aware of these practice-related challenges because the same barriers that hamper optimal administration of food and drink will also hamper medication administration. In repeated observations of “med pass” activities in the long-term care setting, one of the most common medication administration errors is often inappropriate crushing of oral dosage forms. In one evaluation that compared pharmacist observation of the facility med pass, retrospective chart review, and review of facility incident reports, it was the direct observation that was most sensitive to detecting administration errors. Out of a total of 1,423 doses passed, the direct observation method detected 369 errors (25.9%). However, a retrospective chart review only identified documentation of 148 of these occurrences (10.4%). Incident reports captured none. Although most administration errors were evaluated to be minor in severity, a 25% error rate is high, and the most common error type recorded was inappropriate crushing of medications (30.1%). The error rate varied depending on the nurse administering the medications, from zero to a rate of one error every two doses, but all of the nurses who filled out the post-observation questionnaire stated they would be willing to be observed again. These findings support the value of direct observation as the best way to detect administration errors, and they suggest opportunities for interprofessional collaboration for continued staff training, skills assessment, and quality improvement.

Crushed medications should be mixed with a small amount of jelly or similar substance. Jelly is most often preferred because it is an appro-
priate texture and consistency for an individual with dysphagia, the sweetness can help mask the medication taste, and it is commercially available in single-serving size packets that are stable at room temperature. Pudding or similar foods can also work but are often less practical in an institution because of packaging and stability issues. It is important that crushed medication not be mixed into an entire portion of food or drink at a meal, because this requires the patient to consume the entire portion to ingest the intended dose. In addition, this is not appropriate for empty stomach administration instructions, and it is a challenge especially when the crushed medication alters the taste of the food, which may already be less palatable due to puree consistency.

The administration of medication through a tube requires special precautions.\textsuperscript{83} Both liquid and crushed medications have the potential to adhere to or clog the inside of the tube, and consideration must also be given to the timing of medication administration around the infusion of enteral nutrition formulations (usually medications should not be added directly to enteral formulations to avoid contamination and nutrient incompatibilities). In addition to tube obstruction, toxicity or subtherapeutic doses may be consequences of incorrect administration. One study suggested that 74% of hospital staff used at least two incorrect methods for administering medications through a tube.\textsuperscript{84}

If medication administration through a tube is necessary, the first consideration is the type of tube and where it is placed.\textsuperscript{83} The location in the GI tract must be compatible with the site of action/absorption for the medication to be administered. For example, medication expected to act locally in the stomach, such as antacids or sucralfate, would be ineffective if given through a tube terminating in the intestine. The bioavailability of medications undergoing extensive GI first pass can also be increased if given through a tube with an intrajejunal terminus.\textsuperscript{83} These medications include levodopa, beta blockers, nitrates, opioids, and tricyclic antidepressants. Administration of medications through a tube is one scenario where liquid formulations may be preferable if possible (although again, consider total volume and cost when choosing).\textsuperscript{83,85,86} Unfortunately, specific recommendations for administration via tube are not always published for all medications and are often based on clinician consensus.\textsuperscript{86} Several considerations are suggested when deciding how best to administer medication via this route. One such consideration for liquids is the osmolarity of the formulation. For products with an osmolarity of >1,000 mOsm/kg (e.g., acetaminophen, docusate, lactulose, hydroxyzine, ferrous sulfate, multivitamin, lithium, diphenoxylate/atropine), it is recommended to dilute the formulation with 10–30 mL water to avoid side effects such as nausea, cramping, or diarrhea.\textsuperscript{83,85,86}

If crushed medications are to be given, large-bore tubes are preferable, and medications should be given as a slurry with at least 30 mL water to flush the tube before and after administration. For those medications with a narrow therapeutic index, especially those which are likely to adhere to the tube or interact with components of enteral formulations (e.g., phenytoin and warfarin), a more intensive monitoring plan should be implemented to ensure drug therapy outcomes are not compromised with fluctuations in bioavailability.\textsuperscript{83,85,86} In addition, some medications are more reliably administered intravenously if oral administration is not possible. Fluoroquinolones are an example of a medication class for which the bioavailability is usually thought to be similar when given by mouth or intravenously; however, when crushed and administered through a tube, their bioavailability can vary erratically. Intravenous administration may therefore be preferable if possible, but if the fluoroquinolone must be administered through the tube it must be separated by at least 2 hours before or 4 hours after enteral formulations. Moreover, it is recommended that the medication be mixed with a larger volume of water, 20–60 mL, before administration.\textsuperscript{83}
**Special Considerations Affecting Desired Clinical Outcomes**

When medications must be crushed, there are special considerations that the caregiver should be aware of to avoid errors. One such consideration is the teratogenicity of the medication being handled. The medication counseling provided to a male or postmenopausal female patient may not include detailed information about the teratogenicity of the medication, but it should not be assumed that it is the patient alone that would need to handle the medication product during administration. In many care settings, physical contact by the caregiver with the products themselves may be minimal, if any, due to unit-dose packaging that allows the tablet or capsule to be popped directly into a medicine cup. However, this is not true in all settings, and when a medication must be opened or crushed, the likelihood of exposure increases. For many drugs, even those considered pregnancy category X, the degree of absorption through the skin may not be clinically insignificant. However, staff members concerned about risk of exposure should be aware of what they are handling. Regular handwashing after each patient’s medication administration is a part of standard practice; in addition, staff members who are pregnant, trying to become pregnant, or who are breastfeeding may also consider the use of gloves while handling these types of products.

It is also important to be aware of those medications for which crushing is not appropriate but another form of dissolution can be employed. For instance, potassium supplements with extended-release granules suspended in wax matrix should not be crushed, but the wax matrix will readily dissolve, releasing the tiny granules, in a small amount of water. Another example is the opening of proton pump inhibitors (PPIs) to mix the contents with a small amount of an acidic juice. For some capsules containing microencapsulated pellets, the dosage form can be opened and poured down a large bore tube, provided the contents are not crushed. When the pharmacist filling the prescription or providing drug regimen review is aware that a patient may require crushed medications, it may be advisable to recommend auxiliary labeling or special instructions be added to the chart order or the product labeling to flag special administration needs.

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**Gastroesophageal Reflux Disease**

**Etiology, Epidemiology, and Clinical Presentation**

GERD is the most prevalent GI disorder in the United States. Monthly symptoms are reported in >40% of patients and daily symptoms reported in about 10%. Symptons are typically described as heartburn or regurgitation but can also include “extraesophageal” symptoms such as cough, hoarseness or laryngitis, postnasal drip, worsening asthma symptoms, or noncardiac chest pain. Consequences of GERD can include local effects on the esophagus, such as esophagitis, ulceration, bleeding, and Barrett’s esophagus, but GERD can also lead to weight loss, anorexia, and anemia. There are also associations between GERD and exacerbations of chronic obstructive pulmonary disease and insomnia. As such, GERD has a significant impact on overall health, quality of life, and healthcare utilization.

The prevalence of GERD increases with age and is influenced by physiologic changes in the GI tract, including slowed gastric emptying, decreased saliva production, reduced intra-abdominal length of the lower esophageal sphincter, and increased incidence of hiatal hernia. However, symptom presentation is often atypical in frail patients and may be milder or asymptomatic. When symptoms do present, they are often alarm symptoms or may be associated with dysphagia, cough, wheezing, and chest pain. The highest rates of atypical symptoms are reported in the oldest patients, increasing the risk of misdiagnosis or inappropriate prescribing.
KEY POINT: Atypical GERD symptoms can result in polypharmacy if the symptoms are attributed to cardiac, respiratory, or sleep disorders.

GERD can also be caused or exacerbated by medication and food. Drug-induced esophageal injury was discussed in the previous section. Common agents include bisphosphonates, aspirin, NSAIDs, antibiotics, potassium supplements, iron supplements, calcium-channel blockers, theophylline, cholinesterase inhibitors, and antipsychotic medications. The risk of drug-induced GERD increases not only with polypharmacy but with an increased amount of time spent reclining or lying down, and with inadequate fluid intake with medication administration. Common foods associated with GERD include dairy, acidic food such as tomatoes and fruits, fatty foods, caffeine, alcohol, peppermint, and chocolate.

Standard Treatment and Management Strategies in the General Adult Population

Based on recommendations of the American College of Gastroenterology, antacids can be used for intermittent symptoms, but acid suppression therapy is the primary treatment for GERD. PPIs have better efficacy than histamine-2 receptor antagonists (H2RAs), so either a step-up or step-down approach can be employed, depending on the clinical presentation. Step-up therapy employs the H2RA therapy for more mild symptoms with a step up to a PPI. Alternatively, step-down therapy begins more aggressively with the PPI, with higher initial doses prescribed for the healing of ulcers and continued for 6 weeks. The dose may be reduced and ultimately switched to H2RA therapy as symptom control allows.

Evidence Base Supporting Treatment Recommendations in Elderly Patients

In general, the recommendations for treating GERD in elderly patients are similar to those for the general adult population. After the diagnosis of GERD has been made, the selection of appropriate therapy is relatively straightforward; the bigger challenge is often the accuracy of diagnosis and determining appropriate duration of use. GERD can be a chronic or relapsing condition, and, especially in the absence of dietary or nonpharmacological interventions, symptoms can return. However, symptom response to PPI therapy is not necessarily an accurate marker of correct diagnosis, especially among individuals with atypical symptoms, and long-term use of PPIs has also been associated with complications. There are data linking use of acid-suppressing medications to hip fracture. One of the putative mechanisms suggested for this association is reduced absorption of calcium. There are both positive and negative studies published examining the relationship; however, in general, the relationship appears strongest for high-dose, long-term use, especially among frail cohorts at highest risk for fracture.

In addition, chronic acid suppression can alter the natural gut flora, increasing the risk of pneumonia and Clostridium difficile (C. diff.)–associated diarrhea. The association of PPI use with community-acquired pneumonia has been evaluated in a number of settings and suggests that recent (<30 days) or current use of PPI therapy was associated with risk of pneumonia, particularly among frail patients or those with recurrent pneumonia. Elderly patients are already at relatively higher risk of developing C. diff. diarrhea, particularly when treated with antibiotic therapy. However, in addition, the use of acid-suppressing therapy may be an independent risk factor for developing this condition. This association has been evaluated...
in a number of age and ethnic groups.\textsuperscript{112,113} Although one study of older patients in the community setting did not find that PPI use was a risk factor for hospitalization with \textit{C. diff.} diarrhea, the occurrence of a prescription within 90 days of the hospitalization was used as the surrogate for medication use.\textsuperscript{114} Other studies have suggested that PPIs, but not H2RAs, are associated with increased incidence of both first-time and recurrent \textit{C. diff.} diarrhea.\textsuperscript{115,116}

\textbf{Special Considerations Affecting Desired Clinical Outcomes}

For the health professional performing a drug regimen review, it can often be challenging to discern the appropriateness of drug therapy such as chronic PPIs. This class of medication is commonly prescribed in hospitals as part of stress ulcer prophylaxis protocols, often outside the guidelines recommending appropriate scenarios for use.\textsuperscript{117,118} They are frequently used in patients over 60 receiving NSAIDs or co-prescribed with antiplatelet therapy.\textsuperscript{119,120} PPIs are often continued on discharge to the next care venue, whether a skilled nursing unit, long-term care unit, other care environment, or the outpatient setting. Ideally, if standardized guidelines are employed at the time of prescribing, and optimal medication reconciliation and records review are performed on transfer, appropriate medication-indication match could be verified, and the continuation of a medication without long-term indications would not occur.\textsuperscript{117-120} However, where there is lack of adequate documentation, the presence of an underlying indication will often simply be assumed, and while both over- and under-prescribing can occur, a common problem is that the duration of therapy is extended longer than necessary.

Sometimes, the diagnosis is even added to the medical record after the medication therapy is initiated or refilled, making it very difficult for health professionals in the new venue to determine whether discontinuation would be appropriate. There have been multiple publications focusing on the challenges associated with over-prescribing or inappropriate prescribing of PPIs.\textsuperscript{98,117,121} Patients with a recent ulcer or other appropriate diagnosis or whose symptoms have been documented to respond to acid suppression therapy should clearly not be denied access to treatment. However, the long-term continuation of therapy in the absence of a true indication is inappropriate and increases the risk of long-term complications associated with the drug. In addition, patients who remain refractory to PPI therapy should be re-evaluated for nonreflux etiology of symptoms.\textsuperscript{122,123} Meaningful medication reconciliation must be able to verify drug therapy against documentation describing both indication and intended duration of use. Although this is true for any medication prescribed for any reason, it is particularly relative to PPI therapy.

\textbf{KEY POINT:} Medication reconciliation that assesses true medication-indication match is vital to the assessment of appropriate PPI prescribing and duration of therapy.

\section*{Nausea and Vomiting}

\textbf{Etiology, Epidemiology, and Clinical Presentation}

Nausea and vomiting are two of the most common symptoms when someone is ill, and they can occur for many reasons. They are among the top side effects reported with drug therapy and are reported in the product labeling of almost every medication. Nausea and vomiting are especially common with chemotherapeutic agents and opiates, reported in 40% to 90% of individuals treated for cancer and 20% to 40% of individuals treated with opiate analgesics, with much of the data reported in either the palliative or postoperative settings.\textsuperscript{124-130} Nausea and vomiting can be a part of the clinical presentation of many illnesses and part of the atypical clinical presentation of almost any illness exacerbation among frail patients. For example, in addition to
GI illnesses such as gastroenteritis or constipation, pain syndromes, anxiety, thyroid disorders, vestibular disorders, renal or hepatic dysfunction, pancreatitis, cardiovascular events, and syncope can all present with nausea or vomiting. Nausea and vomiting are common after surgical procedures and also near the end of life.\textsuperscript{131,132}

These symptoms have both short- and long-term consequences. The short-term consequences are those almost any individual who has ever been ill can understand: the acute discomfort of being sick to one’s stomach and needing to vomit, associated with stomach cramping, residual muscle pain in the torso following vomiting, and often feelings of dizziness or weakness. Protracted symptoms of nausea and vomiting can take a significant physical and psychological toll, from loss of appetite to significant weight loss and anorexia. This can be associated with dehydration, electrolyte disturbances, physical deconditioning, and functional decline.

**Standard Treatment in the Adult Population**

Treatment requires two approaches: immediate relief of symptoms and removal or at least improvement of the underlying cause of the problem. Either approach is dependent on the etiology of the nausea and vomiting.\textsuperscript{133-136} There are a variety of prescription and nonprescription interventions for symptom treatment, with the primary pharmacological targets being dopamine antagonism (block dopamine receptors in the chemoreceptor trigger zone or increase peristalsis in upper GI tract), 5-HT3 antagonism (block serotonin receptors in the chemoreceptor trigger zone, act at vestibular and vomiting centers), or to block histamine or cholinergic muscarinic receptors (reduce gastric secretions).\textsuperscript{133-136} Commonly employed agents include phenothiazines, droperidol, metoclopramide, anticholinergics, and 5-HT3 receptor antagonists such as ondansetron and granisetron.

**Evidence Base Supporting Treatment Recommendations in Elderly Patients**

The treatment of nausea and vomiting in older patients is often an exercise in balance, as many antiemetic medications carry unfavorable side effects. Ideally, regardless of the agent chosen, drug therapy directed at symptom control is short term while the underlying cause is being addressed. However, if that is not possible, there is a degree of trial and error involved in selecting the antiemetic therapy that effectively relieves symptoms without causing intolerable side effects, a challenge made especially difficult in the presence of comorbidities or polypharmacy. Side effects can be anticipated by understanding the mechanisms of action of the various antiemetic drugs. For instance, dopamine-blocking medications can exacerbate extrapyramidal side effects. One study suggests age is a significant risk factor for sedation, extrapyramidal side effects, and delirium with phenothiazine medication.\textsuperscript{137} Among medications with this mechanism of action, trimethobenzamide is thought to be the least potent antiemetic; therefore, having the least favorable ratio of efficacy to side effect risk.\textsuperscript{138} Metoclopramide can also cause extrapyramidal effects, psychiatric symptoms such as anxiety and depression, somnolence, and cognitive changes, particularly at doses inappropriate for renal dysfunction or when used long term, and it is a common cause of unrecognized drug-induced Parkinson disease.\textsuperscript{139} Antihistaminic or anticholinergic medications can exacerbate sedation, dry mouth, constipation, and cognitive impairment.\textsuperscript{138}

The availability of over-the-counter products used to self-medicate can lead to under-reported nausea and vomiting and under-recognized drug side effects. Agents such as domperidone can prolong the QT interval, whereas droperidol and cannabinoids are more likely to be associated with CNS effects such as dizziness, dysphoria, depression, or hallucination.\textsuperscript{140-142}
5-HT3 receptor antagonists have, in general, a favorable side effect profile but are more costly, and specific trials differentiating their outcomes in frail geriatric patients with non-cancer-related pain have not been published. Applying these considerations may help narrow the choices, depending on the etiology of the nausea and vomiting and the patient's risk factors.

Older patients with cancer require special attention. Individuals over 65 have the highest incidence of cancer, and the course of treatment is often complicated by comorbidity and polypharmacy. However, some evidence suggests that the use of supportive therapy, such as antiemetics, is underutilized.143 The 5-HT3 receptor antagonists are considered first-line for patients at moderate to high risk of nausea and vomiting, and in the highest risk scenarios, combination therapy with 5-HT3 receptor antagonists, aprepitant, and dexamethasone is recommended.144,145 There are no specific guidelines for modifications to this approach for elderly patients; however, there are differences between agents that carry implications for the older patient, especially in the presence of comorbidities. For instance, the product labeling for dolasetron, palonosetron, and tropisetron include warnings for patients with cardiovascular disease. Ondansetron is thought to act at both central and peripheral receptors and may be associated with a higher risk of dizziness or blurred vision.143,144 By contrast, granisetron has fewer CYP450 drug interactions and may be given on a once-daily interval.143 Elderly patients with comorbidities or concomitant NSAID use may also be less likely to receive dexamethasone therapy.146 In the absence of clinical trials specifically evaluating the efficacy and safety of antiemetic therapy in this context, the choice of therapy is unfortunately often empiric.147

**Special Considerations Affecting Clinical Outcomes**

The ability to tolerate oral medication impacts the efficacy of antiemetic therapy for any patient. It cannot be effective if the patient cannot keep it down. Therefore, alternate routes of therapy must often be considered, including orally dissolving, injectable, transdermal, or rectal formulations.

The ability to take oral medication, to keep it down after doing so, or to tolerate it without GI discomfort has direct implications for the long-term control of any medication-treated condition, making adverse drug therapy outcomes both a cause and a consequence of nausea and vomiting. In the long term, changes in nutritional factors, such as albumin or vitamin K stores associated with poor appetite from chronic nausea, also have implications for drugs that are highly bound to albumin or for warfarin sensitivity. When performing a drug regimen review, the pharmacist can use a variety of surrogates to identify whether unrecognized drug-associated nausea syndrome is occurring, such as poor appetite, weight loss, repeated medication refusals, or fluctuations in laboratory parameters. In the long-term care setting, this can be identified from documentation in the chart or the medication administration record, or in the outpatient setting patients can be interviewed regarding reasons for "intelligent nonadherence" to prescribed therapy. The choice to alter or not adhere to therapy may often be associated with previously unreported symptoms. This type of review can also identify possible inappropriate administration techniques causing unnecessary GI distress, such as failure to take bulk-forming laxatives with adequate water. Another could be the administration of NSAIDs on an empty stomach. If modification of the drug, its timing, or its administration technique can alleviate GI distress, this may help avoid therapeutic failure associated with nonadherence.

**KEY POINT:** Drug-induced nausea and vomiting can be “hidden in plain sight.” Careful chart review and/or interview techniques can reveal the common pitfalls in medication use that result in GI distress.
Diverticular Disease

Etiology, Epidemiology, and Clinical Presentation

Aging leads to structural weakness in the colon muscle, predisposing the elderly to diverticular disease. The prevalence of diverticular disease increases from 5% or less in those under age 40 to 65% for individuals over 65.\(^{148}\) Admissions for acute diverticulitis in the United States have increased by 26% from 1998 to 2005.\(^{149}\) The primary risk factor for diverticular disease is a low dietary fiber intake; thus, it is considered a disease of westernized nations. Diagnosis of diverticular disease is most often made on computed tomography; however, barium enema or colonoscopy may also be used in a stable patient.

Diverticulosis refers to the presence of diverticula, or saclike herniation of the colonic mucosa through the muscle, whereas diverticulitis describes an inflammation of one or more diverticula. It is estimated that 80% to 85% of patients with diverticula are asymptomatic. Hemorrhage may occur in 20% of patients and is the most common cause of hematochezia in older adults.\(^{150,151}\) However, acute diverticulitis may cause abdominal pain, bloating, and a change in bowel habits. In addition, for more severe cases of diverticulitis, signs of inflammation such as fever and leucocytosis are present. Acute diverticulitis may be complicated by abscess formation, fistulas, intestinal obstruction, or free perforation with peritonitis. Although perforation is rare, it carries a high mortality of 35%.\(^{148}\) The need for hospital admission is dictated by severity of presentation, comorbidity, and ability to tolerate oral hydration. When acute diverticulitis occurs twice per year or more, it is referred to as recurrent.

Standard Treatment in the Adult Population

A diet high in insoluble fiber is first-line therapy. Insoluble fiber from fruits and vegetables is preferred to that from cereal fibers.\(^{148,151}\) Fiber supplementation can be utilized in those unable to comply with dietary changes, although no large controlled trials support these treatments. A common dose is 30 g of insoluble fiber per day.\(^{152}\) Historically, diets with nuts, corn, or seeds were forbidden in patients with diverticula for fear the particles would lodge in the sac and cause inflammation. However, no data support this pathology, so patients should not be restricted in this manner.\(^{151}\)

Uncomplicated symptomatic diverticular disease may also be treated with a monthly regimen of rifaximin 400 mg twice daily for 10 days or mesalazine 400–800 mg twice daily for 7–10 days. These treatments are off-label but supported by small randomized, controlled trials and are generally reserved for patients with recurrent disease or ongoing symptoms.\(^{152}\)

Severe hemorrhage may occur in 3% to 5% of patients and is more commonly seen in those taking NSAIDs or who are immunocompromised. The bleeding is arterial, usually painless, and should be treated with fluid and blood products as indicated. Bleeding will cease spontaneously in 70% to 80% of patients.

Acute diverticulitis is treated with a clear liquid diet in those patients who are stable and able to tolerate oral intake. A 7–10 day course of metronidazole in combination with trimethoprim/sulfamethoxazole or ciprofloxacin is recommended to cover most anaerobes and gram-negative aerobes. Improvement should be seen in 2–4 days, at which time the diet may be advanced as tolerated. For individuals with more severe disease or who cannot tolerate oral intake, hospitalization is indicated for monitoring electrolyte balance and for more aggressive treatment. These patients should be treated with intravenous fluids and parenteral antibiotics. Coverage of colonic anaerobic and gram-negative flora is needed for 7–10 days.\(^{151}\) Pain management may also be needed with opioid analgesics. Again, clinical improvement is expected within 2–4 days, at which time a diet may be started and the patient converted to oral
antibiotics. Surgical treatment may be necessary in a small subset of patients who develop complications. Elective surgery, sometimes with laparoscopic techniques, is used in patients with recurrent disease after the acute episode has been controlled for several weeks.148,150

**KEY POINT:** NSAIDs are associated with an increased risk of bleeding and perforation in patients with diverticular disease.

### Evidence-Based Recommendations in the Elderly

Few randomized controlled clinical trials are available to support current treatment recommendations for diverticular disease. Trials evaluating the effectiveness of fiber were primarily performed in the 1970s and 1980s and involved small numbers of patients with uncomplicated symptomatic disease.152 Recent meta-analyses indicate rifaximin and mesalamine can provide significant reduction in global symptoms and may reduce acute episodes of diverticulitis. However, most studies were limited to patients age 40–80, and there is a possibility that patients who had irritable bowel syndrome concurrently with diverticular disease were included in the trials.152,153 Nevertheless, the number needed to treat for rifaximin in symptomatic diverticular disease is reported as 3 for symptom relief and is 59 for reduction in complication rate.153

### Special Considerations Affecting Desired Clinical Outcomes

Elderly patients with diverticular disease are more likely to be hospitalized than younger patients because of their significant risk for comorbidity. Surgery is required in 15% to 30%, which carries an additional risk of complications and mortality. Although rare, free perforation with peritonitis carries a mortality rate of 35%. Both perforation and hemorrhage have been associated with NSAIDs, which are frequently used in older patients.152 Antispasmodics are sometimes listed for symptom control of diverticular disease because of their ability to diminish muscular contraction. However, no controlled trials document their benefit, and given their anticholinergic adverse effects, they should be avoided in elderly patients.

### Constipation

**Etiology, Epidemiology, and Clinical Presentation**

Constipation is associated with a decrease in functional ability and quality of life.154 Symptoms or patient complaints include straining, lumpy or hard stools, sensation of incomplete evacuation, sensation of obstruction or blockage, and manual maneuvers to facilitate defecation.155 Whereas approximately 12% of individuals in North America report having had chronic constipation, the prevalence increases to 16% to 26% in patients over age 65 and further increases to 26% to 34% in patients over age 84.156,157 A more striking statistic is that 50% to 79% of nursing home residents have constipation and/or take a laxative on a daily basis.155 Prevalence varies due to the different definitions of constipation. It was once defined as fewer than three bowel movements per week, whereas the definition now includes hard stools and straining. The latter is often more important to patients who may continue to complain of constipation if they strain or have hard stools, regardless of the number of bowel movements they have in a week. On the other hand, some patients erroneously believe that a daily bowel movement is important for colon health and request laxatives to achieve this goal.157

In addition to the symptoms of straining, incomplete evacuation, and hard stools, patients may have abdominal pain, dysuria, and incontinence (both fecal and urinary). Delirium or agitation may be the presenting symptom, most often seen in patients with degenerating mental illnesses. Complaints of anorexia and nausea
can be associated with constipation, especially if **fecal impaction** develops. Bed-bound patients who are unable to express complaints may react to the discomfort of constipation by fingerling, rubbing, or scratching the anus, resulting in the unhygienic spread of stool.

Primary constipation may be caused by disordered defecation, where the relaxation of the pelvic floor and the sphincters during the process of defecation is not coordinated. Another primary cause is slow transit constipation, identified by use of radio-opaque pills or a wireless motility capsule that measures colonic transit time, pH, temperature, and pressure. However, the most common type of primary constipation in elderly patients is functional constipation. There are many secondary causes of constipation. Lifestyle factors, such as a diet poor in fiber or low activity levels, are common. Metabolic, endocrine, or GI diseases; neurogenic or psychogenic disorders; and medications are frequently cited. These underlying factors must be carefully assessed because they guide subsequent management.

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**Standard Treatment in the Adult Population**

Clinical evaluation starts with the patient’s description of his or her constipation. Specific alarm symptoms include hematochezia, melena, family history of colon cancer or inflammatory bowel disease, anemia, weight loss, nausea, and vomiting. Patients reporting any of these conditions may require additional evaluation with colonoscopy for underlying life-threatening conditions. However, these symptoms are uncommon with typical chronic constipation. A rectal examination may identify sphincter or pelvic floor abnormalities associated with disordered defecation. Laboratory testing is not routinely necessary unless a specific organic disorder is suspected. Correction of underlying diseases that contribute to constipation should be attempted.

The best treatment for constipation in younger adults is prevention through increased dietary consumption of fruits, vegetables, and cereals. Dietary habits should be thoroughly scrutinized to identify the usual amount of fiber consumed. Over-the-counter bulk-forming laxatives may be used to supplement dietary fiber. Stool softeners may aid patients with hard stools or straining. Although some evidence supports supplementation of the diet with bran, yogurt, or psyllium, the data are not strong. Similarly, the use of docusate has not been shown in well-controlled trials to improve the number of stools or their consistency. However, these lifestyle changes and medications are generally well tolerated, and many patients do report favorable results.

If a patient has not had a bowel movement in the past 3–4 days, acute relief is needed. This may be obtained most quickly with stimulants or enemas. The osmotic agents (lactulose, magnesium hydroxide, polyethylene glycol) have fair-to-good studies supporting their effectiveness and offer fairly rapid results, usually within 6–12 hours. However, these agents are not without risk, so patients should be taught that lifestyle changes are the primary method of prevention and treatment of constipation, and stimulant or osmotic laxatives should only provide acute relief.

Lubiprostone is a chloride channel activator that stimulates fluid secretion into the colon. Clinical trials in adults show an increase in stool frequency and a reduction in straining and constipation severity. However, it is relatively expensive when compared to other laxatives and is primarily used in refractory constipation. The opioid receptor antagonists alvimopan and methylnaltrexone are also expensive and used primarily in hospitalized patients after surgery or in palliative care. They offer the advantage of not crossing the blood-brain barrier, so they do not counteract analgesia or precipitate withdrawal.

Special circumstances dictate specific treatments. Individuals taking opiate analgesics or with neurogenic causes of constipation will require routine use of stimulant laxatives.
Individuals with disordered defecation may respond to biofeedback therapy, so that as coordination improves over time, laxative use can be reduced. Of course, a thorough assessment of medications that contribute to constipation should be performed and steps to stop or decrease doses, when appropriate, should be implemented.

**Evidence Base Supporting Treatment Recommendations in Elderly Patients**

Assessment of elderly patients for constipation should include evaluation for depression, hypothyroidism, hypercalcemia, hypermagnesemia, and GI bleeding. Any identified diseases that can contribute to constipation should be appropriately managed. In guiding treatment, clinicians should consider whether fecal impaction is present.

**KEY POINT:** Fecal impaction is linked to delirium and can progress to intestinal obstruction if left untreated.

Elderly patients have been represented in most trials of laxatives for treatment of constipation. Therefore, management in the older population closely follows that for younger adults, especially in healthy community-dwelling elderly patients. Recommendations for therapy in bed-bound elderly patients follow a different pathway. A statistically significant improvement in constipation has not been shown in this subgroup when treated with fiber, bulking agents, and/or stool softeners in comparison to placebo. However, osmotic agents such as polyethylene glycol, magnesium hydroxide, lactulose, and sorbitol were superior to placebo in nursing home residents, including nonambulatory patients. Placebo-controlled trials are lacking for senna and bisacodyl in both community-dwelling and institutionalized older adults. However, they are still recommended for acute relief of constipation in older adults and for routine scheduled use when needed.

**KEY POINT:** The most important assessment in elderly patients with constipation is a medication regimen review.

Probiotics such as *Lactobacillus* and *bifidobacterium* are not currently recommended for routine use in treatment or prevention of constipation. Although some studies exist, they are generally not well controlled, and issues with the viability and variability of the tested product continue to be raised. Likewise, studies with traditional Chinese medicines containing hemp seed, acupuncture, and herb combinations are heterogeneous and difficult to apply to practice.

**Special Considerations Affecting Desired Clinical Outcomes**

When performing an assessment of delirium and agitation in elderly, cognitively impaired patients, clinicians should consider constipation as a cause or contributing factor. One study identified constipation associated with physical aggression in nursing home residents, with an adjusted odds ratio of 1.3 (confidence interval 1.2–1.5). An abdominal examination and x-ray to identify the presence of stool are indicated when a change in behavior or level of consciousness is noted.

Iron, opiates, agents with anticholinergic activity, and calcium channel blockers are frequent offenders; however, many agents may contribute. Ferrous sulfate 325 mg should not be dosed more than once daily because of the increase in risk for GI problems without substantial increase in the amount of iron absorbed. Calcium-channel blockers contribute to disordered defecation and have been named the most common unrecognized cause of constipation.

Many elderly patients are seen in the emergency department with fecal impaction because proper steps to prevent or treat constipation were not implemented quickly enough. In these patients, fiber and bulk-forming agents are inappropriate. Manual disimpaction, enemas, and/or suppositories should be utilized to break up...
the hard stool and enable its passage out of the colon and rectum. Tap water enemas are preferred, as soap suds enemas have been linked to rectal mucosal irritation and phosphate enemas increase the risk for acute kidney injury.

The group of patients most commonly associated with laxative abuse is young adults with eating disorders. However, older adults are also likely to abuse laxatives. In this group laxative use begins as a legitimate treatment for constipation or is associated with a belief that good health requires a daily bowel movement. With daily use, especially with stimulant laxatives, patients become dependent. The clinician must identify the patient's beliefs regarding bowel movements and laxative use and provide education where needed. A laxative withdrawal protocol may be helpful, switching from stimulant laxatives to fiber and magnesium hydroxide laxatives. Behavioral therapy may be needed in conjunction with the changes.

Fecal Incontinence

Etiology, Epidemiology, and Clinical Presentation

Fecal incontinence is the involuntary loss of liquid or solid stool, although some studies include flatus, and others further specify that the loss results in social or hygienic problems. In addition, 50% to 70% of people with fecal incontinence also report urinary incontinence, and this combination is the second most common cause of placement in long-term care facilities. In community-dwelling older adults, the prevalence of fecal incontinence is reported to be as high as 36% compared to 33% to 65% in elderly patients residing in nursing homes. Predisposing conditions in elderly patients include diabetes mellitus, irritable bowel syndrome, and multiple sclerosis.

Many patients with fecal incontinence are anxious or embarrassed and will not initiate discussion about the problem with their healthcare providers, or they may identify it as diarrhea instead. Passive treatment of fecal incontinence with use of pads seems to be the usual treatment for both community-dwelling elderly patients and nursing home residents. A more rational approach would include a medical review of potential causes and treatment tailored to the cause. The most common cause of fecal incontinence in elderly nursing home patients is fecal impaction and overuse of laxatives, which can be controlled and prevented.

Standard Treatment in the General Adult Population

In younger adults, fecal incontinence is frequently the result of trauma, usually from vaginal delivery or surgery, which causes dysfunction of the anal sphincters or pelvic floor. Testing of anal pressures, sensation, or nerve conduction may be performed to characterize the problem and guide therapy. Bulking agents such as methylcellulose are used to improve stool consistency. Antidiarrheal drugs and anticholinergic agents aid in reducing stool frequency.

Supportive measures include the avoidance of caffeine, no exercise after eating, ritualizing bowel habits, and good perineal skin hygiene, as this care is known to improve symptoms. These recommendations are also useful in elderly patients. Biofeedback therapy helps to retrain the pelvic floor and improve muscle strength so that a coordinated effort to defecate occurs. Evidence of effectiveness is controversial, and patients must be cognitively intact to benefit. In some instances, injection of collagen, silicone, or dextranomer/hyaluronic acid around the internal anal sphincter may be indicated after conservative measures are found to be unsuccessful. Surgical repair of damage from trauma may be an option, and colostomy would be considered a last resort.

Evidence Base Supporting Treatment Recommendations in Elderly Patients

Few high-quality trials are performed in the area of fecal incontinence, and fewer still include significant numbers of older subjects. The find-
ings from the International Consultation on Incontinence Management of Fecal Incontinence in Adults Committee produced no Grade A recommendations but relied mainly on expert consensus for its conclusions. The recommendations include optimization of stool consistency, consideration of alternative medications in medication-induced diarrhea, toilet access, education of patients and caregivers, bowel training, and biofeedback in addition to use of laxatives with impaction or antidiarrheals in diarrhea. In particular, they note that fecal incontinence in frail older people should be evaluated through direct questioning and observation, so that active treatment can be tailored to the patient.\textsuperscript{166}

In one open-label study of 82 nursing home residents from 30 facilities, subjects were assessed as having fecal incontinence due to impaction/constipation or due to neuromuscular dysfunction. Individuals with impaction/constipation received treatment with regular toileting after meals and lactulose 10 mL twice daily plus a weekly enema. Individuals with neuromuscular dysfunction received regular toileting after meals and codeine 30–60 mg daily. These two groups were compared to a control group of 30 patients. The investigators reported a cure rate of 87% compared to 32% of the control group.\textsuperscript{167} Although an older study, this information supports institution of conservative measures tailored to the suspected cause of the incontinence.

**KEY POINT:** When fecal impaction is treated with oral laxatives, seepage of stool around the blockage can occur and mimic incontinence.

### Special Considerations Affecting Desired Clinical Outcomes

Elderly adults are not as likely as younger adults to have fecal incontinence due to trauma, so the approach to an older patient is different. A focused medical history and physical examination will frequently identify the cause of fecal incontinence in the elderly patient. In older adults, the three most common categories that guide therapy are fecal impaction, diarrhea and urgency, and neuromuscular dysfunction.\textsuperscript{168}

The first and most common category is fecal impaction. Incontinence occurs because impaction produces inhibition of sphincter tone. When this is coupled with laxative use, seepage of stool occurs around the blockage. This etiology is reported in 42% of older adults with incontinence.\textsuperscript{164} Its treatment involves manual disimpaction and enemas. After the impaction is resolved, preventive measures should be instituted, such as avoidance of constipating medications, increased mobility, and routine use of laxatives.

The second category includes diarrheas from infection, colitis, inflammatory bowel disease, or radiation therapy. Treatment of the underlying condition will usually resolve the incontinence. Diarrhea may also result from use of medications, as shown in Table 11-1.\textsuperscript{169} Alternative agents should be considered for use, when possible. If necessary, treatment with fiber and antidiarrheals can be implemented. Loperamide is preferred over diphenoxylate/atropine or codeine because of reduced adverse effects.

### Table 11-1. Commonly Used Drugs Causing Diarrhea in Elderly Patients

<table>
<thead>
<tr>
<th>Category</th>
<th>Drugs</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>ANTIMICROBIALS:</strong></td>
<td>Cephalosporins, clindamycin, penicillins, tetracyclines, quinolones, macrolides, interferon</td>
</tr>
<tr>
<td><strong>CARDIOVASCULAR AGENTS:</strong></td>
<td>Angiotensin-converting enzyme inhibitors, beta blockers, digoxin, erythropoietin analogues, furosemide, hydralazine, quinidine, spironolactone, ticlopidine</td>
</tr>
<tr>
<td><strong>CENTRAL NERVOUS SYSTEM AGENTS:</strong></td>
<td>Acetylcholinesterase inhibitors, carbamazepine, selective serotonin receptor inhibitors, anticonvulsants</td>
</tr>
<tr>
<td><strong>ENDOCRINE AGENTS:</strong></td>
<td>Acarbose, bisphosphonates, calcitomin, metformin, thyroid hormones</td>
</tr>
<tr>
<td><strong>GASTROINTESTINAL AGENTS:</strong></td>
<td>Esomeprazole, lactulose, sorbitol, magnesium-containing antacids, metoclopramide, misoprostol, octreotide, orlistat, polyethylene glycol</td>
</tr>
<tr>
<td><strong>OTHER:</strong></td>
<td>Antineoplastic agents, azathioprine, colchicine, NSAIDs, theophylline</td>
</tr>
</tbody>
</table>

*Source:* Data from references 165 and 169.
Finally, anorectal neuromuscular dysfunction from neuropathy, previous surgery, or injuries should be considered. In these situations, it is recommended to use insoluble fiber to increase the bulk of the stool, with toileting after meals. The next step is to train the patient through behavioral therapy or biofeedback if he or she is able to participate in the process. Injection procedures and surgical techniques may be indicated in selected patients.

No matter what type of fecal incontinence is identified, skin breakdown must be assessed in the older adult. Presence of moisture may lead to pressure sores, given the vulnerability of older skin; these sores are apt to become infected with organisms introduced by fecal matter. In addition to frequent diaper changes, preventive use of zinc oxide or hydrocolloids as a moisture barrier is indicated.

**Clostridium difficile Diarrhea**

**Etiology, Epidemiology, and Clinical Presentation**

*C. diff.* has been recognized as the culprit in 30% of antibiotic-associated diarrhea cases and is the most common cause of infectious diarrhea in hospitalized patients. It is a gram-positive anaerobic bacillus that can form spores. Its spore-forming ability can impair efforts to eradicate the infection. Exposure to broad-spectrum antibiotics allows overgrowth of *C. diff.* in the intestine of colonized hosts, causing diarrhea through formation of enterotoxins that increase inflammation and friability of the intestinal wall.

The median onset of diarrhea after exposure to *C. diff.* and antibiotics is 2–3 days. The diarrhea may be a relatively mild acute onset of watery stools, or it may include abdominal cramping, low-grade fever, and leukocytosis. If the white blood cell count exceeds 15,000 cells/µL, or the serum creatinine rises more than 150%, experts identify this as severe infection. Hypotension, shock, ileus, or megacolon may complicate *C. diff.* infections, potentially leading to death. Mild-to-moderate disease lasting <10 days in older adults is seen in 60% of older adults, but 32% had illness lasting a mean of 18 days, and 8% had severe colitis or other complications.

The Centers for Disease Control and Prevention reports an annual incidence of *C. diff.* infection of 250,000 hospitalizations each year, with a mortality rate of 1% to 2.5%. Outbreaks of more severe disease have been observed during 2002–2006 and were attributed to increases in fluoroquinolone use and the development of a particular strain of *C. diff.* referred to as NAP1/BI/027. This strain has an increased virulence and a higher level of resistance to fluoroquinolones. Rates of hospital discharge with a diagnosis of *C. diff.* infection are more than fivefold higher for individuals over 65 than for those age 45–64.

The most important risk factor for *C. diff.* infection is advanced age. This may be partly due to the age-related effects on immune defense, including decreased gastric acidity, diminished antibody response to toxins, and impaired phagocytosis. An important modifiable risk factor is exposure to antibiotics, identified in over 96% of cases. Clindamycin and cephalosporins are more associated with *C. diff.* diarrhea than other antibiotics, but any broad-spectrum antibiotic or combination of antibiotics will predispose a patient to develop *C. diff.* infection. Additional risk factors are hospitalization or residence in a nursing home or skilled nursing facility. Somewhat controversial is whether use of PPIs or H2RAs increases risk for *C. diff.* infection. Theoretically, the lack of stomach acid may allow passage of *C. diff.* or its spores through the stomach without being destroyed, thus predisposing the patient to infection. PPIs have been associated with recurrent disease, but studies for initial infection are less convincing, probably due to the confounding use of antimicrobials in a high percentage of patients. For the risks associated with PPIs and *C. diff.* diarrhea, see Gastroesophageal Reflux Disease in this chapter.

**Standard Treatment in the General Adult Population**

Nonpharmacologic treatment begins with discontinuing predisposing antibiotics and
in adults. It offers an alternative to metronidazole and vancomycin. In comparison with oral vancomycin, fidaxomicin had a lower rate of recurrence. At present, due to its cost, the drug is not considered first-line therapy but may be used if a patient has a high risk for recurrence and rehospitalization. Additional alternatives include nitazoxanide, rifaximin, and tigecycline. Some data indicate that rifaximin may offer an advantage to prevent *C. diff.* diarrhea recurrence. Intravenous tigecycline has been shown effective in a case series of patients with severe refractory disease and, thus, offers a parenteral alternative to metronidazole.

### Evidence Base Supporting Treatment Recommendations in Elderly Patients

Most studies in the treatment of *C. diff.* infection generally include subjects over age 65, as the disease is highly prevalent in the elderly. For example, testing of the new agent fidaxomicin was performed with 50% of subjects over age 65 and 31% over age 75. However, individuals with life-threatening disease or toxic megacolon were excluded. A primary reservoir of *C. diff.* are long-term care facilities. Several reports of environmental contamination and outbreaks in nursing homes provide evidence of this.

As noted, older age is the most frequently named risk factor for *C. diff.* infection, with an incidence in hospitalized adults over the age of 65 years old 5–10 times as high as younger adults. Elderly patients are frequent recipients of antibiotics and experience prolonged institutionalization. Use of feeding tubes and acid-suppressant medications may contribute to their risk of *C. diff.* infection. The severity of infection in the elderly is dramatically higher probably because of comorbid conditions and age-related changes in host defenses. The most frequently identified cause of acute infectious diarrhea in the nursing home is *C. diff.*, and guidelines for hospitals have been adapted to provide recommendations for prevention and control.
**KEY POINT:** Pharmacists in hospitals and nursing homes may be called on to aid in antimicrobial stewardship, reduction in acid-suppressant therapy, selection of proper therapy, and choosing disinfectants for use with fomites and the inanimate environment to reduce the spread of *C. diff*.

**Special Considerations Affecting Desired Clinical Outcomes**

With elderly patients it is most important for the clinician to have a high index of suspicion for *C. diff.* infection when an acute diarrhea occurs, especially if patients are known to have been exposed to antibiotics within the past 8 weeks. However, older, frail patients are more likely to have severe *C. diff.* infection and may present with ileus or toxic megacolon instead of diarrhea. Enzyme immunoassays for *C. diff.* enterotoxins have a sensitivity of 70% to 85% and a specificity of 95% that does not preclude a negative toxin test in the presence of a *C. diff.* infection.\(^{171}\)

Appropriate therapy for elderly patients may require lower doses of metronidazole, especially in the face of renal or liver impairment. Long-term use is associated with irreversible toxicity; therefore, patients who have more than one recurrence should be treated with alternative agents instead of repeated courses of metronidazole.\(^{172}\)

Recommended doses of oral vancomycin are 125 mg, although in severe disease higher doses may be prescribed. Vancomycin capsules are expensive, so some pharmacies may compound oral solutions from the intravenous vancomycin powder. Proper techniques and labeling are required to prevent medication errors with this practice. For patients with ileus or toxic megacolon, experts recommend rectal instillation of vancomycin combined with intravenous metronidazole.

Studies of the efficacy and safety of probiotics for prevention and treatment of *C. diff.* infection have conflicting results. Most studies of lyophilized *Saccharomyces boulardii* when used with the initial antibiotic regimen in prevention of *C. diff.* infection are favorable. However, the heat-dried product has stability issues and must be refrigerated, limiting its likely effectiveness. Use of *S. boulardii* as treatment or in recurrent infection is not supported by good clinical studies.\(^{174}\) Furthermore, risk for development of fungemia is higher when this product is used in immunocompromised patients, patients in the intensive care unit, and patients with central venous catheters; therefore, it is not recommended in these settings.\(^{172}\) *Lactobacillus* has some small case series that support its use, but bacteremia has been reported. Further study is required before it can be recommended for routine use.\(^{172}\)

Fecal transplantation has been successful in curing older adults with recurrent *C. diff.* infections, with an 89.6% remission rate. Relapses occurred with recurrent antibiotic use or in the presence of the highly virulent NAP1/B1/027 strain.\(^{175}\)

**Nutrition**

**Etiology, Epidemiology, and Clinical Presentation**

Nutritional needs change as a part of normal aging. Nutritional risk increases dramatically for this population when these changes are coupled with an increase in the number and severity of diseases and their associated therapies. It is common for older adults to become more sedentary and lose lean body mass as they age and to compensate with a corresponding reduction in caloric intake. However, because of changes in micronutrient absorption, disease and drug effects, and changes in protein breakdown, malnutrition may develop with a reduction in intake. The prevalence of undernutrition is high in older adults, ranging from 14% to 27% in community-dwelling persons and from 25% to 85% of nursing home residents.\(^{176}\)

Involuntary weight loss may occur if caloric or protein intake does not meet expenditures. Inadequate dietary intake may also be a result of
social factors. Many elderly patients live alone, and individuals who eat alone tend to eat less than those who have socialization at mealtimes. Depressed patients also may eat less. Fixed incomes may inhibit a retiree from buying food when money is needed for basic utilities or medications.

Medical conditions such as dysphagia, chewing difficulties, paralysis from stroke, or dementia can prevent individuals from consuming adequate nutrition. Anorexia is common with many illnesses, especially dementia and mood disorders. Medications may further impair an older adult’s ability to eat or may reduce appetite. Additional physiologic changes that occur with aging contribute to decreased intake, including a reduction in taste and smell so foods are not as appetizing as they once were. Older adults have early satiety due to changes in gastric emptying and changes in cholecystokinin and leptin release.

A second common etiology of involuntary weight loss in elderly patients is cachexia, a syndrome of severe weight, fat, and muscle loss accompanied by elevated protein catabolism secondary to an underlying disease. Inflammation from diseases such as cancer; obstructive lung disease; acquired immunodeficiency syndrome (AIDS); rheumatoid arthritis; and heart, liver, or renal failure produces cytokines that cause a dysregulation between catabolism and anabolism. Anorexia is a common symptom also associated with the cachexia syndrome.

The loss of muscle mass and strength that occurs with aging and is responsible for functional impairment is called sarcopenia. It is commonly diagnosed by the presence of (1) muscle mass two or more standard deviations below normal (adjusted for sex and ethnicity) in young adults, and (2) diminished walking speed (below 0.8 miles/sec). Although there is overlap between cachexia and sarcopenia, the most common distinguishing feature is that sarcopenia is not associated with a particular inflammatory disease. Comorbidities or inadequate nutritional intake may be present and contribute to the development of sarcopenia. It is currently thought that sarcopenia develops through a combination of effects from reductions in testosterone and estrogen, increased insulin resistance, reduced physical activity, and inadequate protein intake.

Overnutrition also occurs in older adults, as defined by body mass index (BMI) of 25–29.9 (overweight) or >30 (obesity). Obesity is reported in 37% of men over age 60 and 42% of women over age 60. Overnutrition is associated with increased mortality and a number of diseases in the population as a whole. However, several studies have shown that overweight and obesity do not increase mortality in older adults except perhaps at the highest levels (BMI above 35). For example, a cohort study of nearly 21,000 community-dwelling Medicare recipients showed a U-shaped curve for mortality, with increased mortality above expected in those with a BMI below 18.5 or above or equal to 35. No increase in mortality was seen for those with an overweight BMI or an obese BMI between 30 and 34.9. However, overweight and obesity were associated with increasing disability.

**KEY POINT:** Low body weight carries a worse prognosis for elderly patients than overweight or obesity.

**Evidence Base Supporting Treatment Recommendations in Elderly Patients**

For elderly patients who are overweight (BMI 25–29.9) without significant disability, weight loss is not generally recommended as individuals in this range do not show an increased overall mortality. Likewise, weight loss in older patients with obesity may not influence mortality. However, weight loss can be an effective means to reduce cholesterol, blood pressure, blood glucose, obstructive sleep apnea, and osteoarthritic knee pain. When older adults are recommended or choose to lose weight, the strategy
is different than in younger adults. A physician should evaluate the patient for underlying issues and to identify appropriate exercise levels. As in younger adults, weight loss programs in elderly patients are unlikely to be successful if exercise is not an important component. Additional protein should be included in the diet along with sources of vitamin D, calcium, vitamin B12, fiber, and fluids. Fad diets have a greater potential for harm in the older adult, especially if concomitant diseases are present.\textsuperscript{181}

Nutritional screening evaluating undernutrition for older adults can be accomplished by measuring weight and height, by monitoring for weight loss, and through nutritional screening tools. If body weight is below 80% of the recommended weight or the BMI is \textless 18.5, further evaluation is recommended. Unintentional weight loss merits further assessment when it exceeds 4.5 kg over 6 months. Alternatively, a threshold based on percentage of baseline body weight may be used: 2% over 1 month, 5% over 3 months, or 10% over 6 months. Finally, several screening questionnaires have been developed. The Mini-Nutritional Assessment has been validated in older adults, has been shown to correlate with outcomes, and is widely used (see Figure 11-1). A short form and a self-administered questionnaire are also available online along with corresponding instruction manuals and a smartphone application at http://www.mna-elderly.com/mna_forms.html. These screening tools aid the clinician in focusing on specific issues in the evaluation.\textsuperscript{182}

In general, evaluation of an older adult who has been screened to have undernutrition begins with a complete history. Medications that may cause changes in taste should be identified and discontinued, if possible. A complete blood count, basic metabolic panel, albumin, C-reactive protein, and thyroid-stimulating hormone are laboratory tests that may help identify treatable underlying conditions. Malignancy should be suspected, especially in patients with involuntary weight loss. The likelihood of malignancy is further increased in patients over 80, with an elevated white blood cell count, a decreased albumin, or elevated alkaline phosphatase or lactate dehydrogenase.

If underlying diseases are not found, general treatment for sarcopenia is needed. Dietary restrictions such as low salt and low cholesterol diets should be removed. Some patients with sarcopenia may still have diabetes, with elevated blood glucose. Their diets should be liberalized with only limits on concentrated sweets. Hypoglycemic medication doses can be increased to control blood sugars rather than limit the diet of patients who are losing weight or muscle mass. Food choices should be tailored to patients’ ethnic or cultural preferences to encourage increased intake.

Patients should be evaluated for the ability to feed themselves and ability to obtain food. In long-term care settings, many dementia patients lose the ability to feed themselves and will eat a healthy diet when assisted with feeding. Other patients with stroke, Parkinson disease, or benign essential tremor may be able to feed themselves with appropriate silverware or medications to control movements. Economic assistance may be all that is necessary to improve the diet of patients who cannot afford their food. Meal or food delivery services are helpful for individuals unable to shop for groceries if family or caregivers cannot fulfill this need. Bringing elderly patients together for meals is preferable to having them eat alone, as studies show more is consumed in social settings.

Supplementation of oral intake is the next component of the treatment plan. Some high-calorie snacks may be appetizing and provide the added calories and protein needed. For example, one piece of bread with 1 tablespoon each of peanut butter and jelly eaten with 1 cup of 2% milk yields 320 calories and 15 g of protein. Similar snacks or nutrient-dense meals can be concocted from hard-boiled eggs, Greek yogurt, and instant breakfast powders, and are relatively inexpensive.\textsuperscript{183} Oral meal replacements and supplements are another alternative and have been shown to increase weight in patients living at home, in long-term care, and
**Mini Nutritional Assessment (MNA®)**

**Last name:**  
**First name:**

**Sex:**  
**Age:**  
**Weight, kg:**  
**Height, cm:**  
**Date:**

Complete the screen by filling in the boxes with the appropriate numbers. Add the numbers for the screen. If score is 11 or less, continue with the assessment to gain a Malnutrition Indicator Score.

### Screening

**A** Has food intake declined over the past 3 months due to loss of appetite, digestive problems, chewing or swallowing difficulties?
- 0 = severe decrease in food intake
- 1 = moderate decrease in food intake
- 2 = no decrease in food intake

**B** Weight loss during the last 3 months
- 0 = weight loss greater than 3kg (6.6lbs)
- 1 = does not know
- 2 = weight loss between 1 and 3kg (2.2 and 6.6 lbs)
- 3 = no weight loss

**C** Mobility
- 0 = bed or chair bound
- 1 = able to get out of bed / chair but does not go out
- 2 = goes out

**D** Has suffered psychological stress or acute disease in the past 3 months?
- 0 = yes
- 2 = no

**E** Neuropsychological problems
- 0 = severe dementia or depression
- 1 = mild dementia
- 2 = no psychological problems

**F** Body Mass Index (BMI) (weight in kg) / (height in m²)
- 0 = BMI less than 19
- 1 = BMI 19 to less than 21
- 2 = BMI 21 to less than 23
- 3 = BMI 23 or greater

Screening score (subtotal max. 14 points)
- 12-14 points: Normal nutritional status
- 8-11 points: At risk of malnutrition
- 0-7 points: Malnourished

For a more in-depth assessment, continue with questions G-R

### Assessment

**G** Lives independently (not in nursing home or hospital)
- 1 = yes
- 0 = no

**H** Takes more than 3 prescription drugs per day
- 0 = yes
- 1 = no

**I** Pressure sores or skin ulcers
- 0 = yes
- 1 = no

### References

4. Société des Produits Nestlé, S.A., Vevey, Switzerland, Trademark Owners  

For more information: www.mna-elderly.com

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**Figure 11-1.** The Mini-Nutritional Assessment (MNA).

in hospitals. However, functional status is less responsive. Mortality reduction has been shown in hospitalized undernourished patients with supplementation. Boost, Magic Cup, Glucerna, and Ensure are common brand names frequently used. In addition, most sources recommend a geriatric multivitamin with minerals supplement given daily. Some studies show a decrease in infections for older adults taking multivitamins with minerals; however, a recent large cohort study of older women showed a small increase in mortality for those taking daily multivitamins (hazard ratio 1.2, 95% CI 1.02–1.10).^{184,185}

Appetite stimulants are sometimes prescribed for older adults to help with weight gain. Dronabinol is indicated for AIDS-related anorexia. Little evidence exists in elderly populations, and in general it is not well tolerated due to the CNS effects.

Megestrol acetate has been shown modestly effective for cachexia associated with cancer or AIDS in younger adults. A few studies exist in elderly patients without these disorders, and results have been mixed, with some patients adding weight and others not. The weight is not uniformly shown to be lean body mass; therefore, it is unclear that the risk for adverse effects (e.g., deep-vein thrombosis, adrenal axis suppression) is outweighed by its efficacy. Doses commonly prescribed are 400–800 mg per day, which is difficult to achieve with tablet formulations. Usually, the oral suspension is used to achieve this dose.^{186}

Mirtazapine is also used for appetite stimulation as it possesses histamine-1 receptor antagonism. Dosing begins at 7.5 mg at bedtime and may be increased to 15 mg. Studies have focused on weight gain in patients with concomitant depression or dementia with depression and show an increase of 2–4 kg over 6 weeks. However, this is not significantly different from other antidepressants when used to treat depression. Evidence of efficacy is not available for undernourished patients without depression.^{186} Given the generally favorable adverse effect profile of mirtazapine, it remains a reasonable choice for patients with weight loss that is associated with depression. The use of mirtazapine as an appetite stimulant in individuals without depression has not been sufficiently evaluated.

**Special Considerations Affecting Desired Clinical Outcomes**

The Institute of Medicine has recommended dietary intakes for macronutrients, vitamins, and minerals. Those recommendations are different in older adults because of changes in physiology and overall food intake. In general, protein intake recommendations are 0.8 g/kg per day to make up 10% to 35% of total calories to maintain muscle mass equilibrium. Older adults who need to build muscle mass require 1–1.2 g/kg. Energy needs tend to decrease with aging because of lower muscle mass and an increased sedentary lifestyle. The calories derived from carbohydrates and fat would be reduced as physical activity decreases; however, a minimum amount from carbohydrates is needed to maintain brain function. Table 11-2 provides the dietary reference intakes of macronutrients and selected micronutrients for older adults.^{187} These are considered minimum values.
Table 11-2. Selected Dietary Reference Intakes for Older Adults

<table>
<thead>
<tr>
<th>Macronutrients</th>
<th>Energy (kcal)</th>
<th>Protein (g)</th>
<th>Carbohydrates (g)</th>
<th>Total Fat (% kcal)</th>
<th>Fiber (g)</th>
<th>Water (L)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age 51–70 Male</td>
<td>2204</td>
<td>56</td>
<td>130</td>
<td>20–35</td>
<td>30</td>
<td>3.7</td>
</tr>
<tr>
<td>Age 51–70 Female</td>
<td>1978</td>
<td>46</td>
<td>130</td>
<td>20–35</td>
<td>21</td>
<td>2.7</td>
</tr>
<tr>
<td>Age 70+ Male</td>
<td>2054</td>
<td>56</td>
<td>130</td>
<td>20–35</td>
<td>30</td>
<td>2.6</td>
</tr>
<tr>
<td>Age 70+ Female</td>
<td>1873</td>
<td>46</td>
<td>130</td>
<td>20–35</td>
<td>21</td>
<td>2.1</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Selected Vitamins and Minerals</th>
<th>Vitamin D (mcg)</th>
<th>Vitamin B12 (mcg)</th>
<th>Calcium (mg)</th>
<th>Iron (mg)</th>
<th>Magnesium (mg)</th>
<th>Zinc (mg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age 51–70 Male</td>
<td>10</td>
<td>2.4</td>
<td>1200</td>
<td>8</td>
<td>420</td>
<td>11</td>
</tr>
<tr>
<td>Age 51–70 Female</td>
<td>10</td>
<td>2.4</td>
<td>1200</td>
<td>8</td>
<td>320</td>
<td>8</td>
</tr>
<tr>
<td>Age 70+ Male</td>
<td>15</td>
<td>2.4</td>
<td>2500</td>
<td>8</td>
<td>420</td>
<td>11</td>
</tr>
<tr>
<td>Age 70+ Female</td>
<td>15</td>
<td>2.4</td>
<td>2500</td>
<td>8</td>
<td>320</td>
<td>8</td>
</tr>
</tbody>
</table>

*Source: Data from National Policy and Resource Center on Nutrition and Aging. Florida International University.*187
CASE 1: HOSPITAL GERIATRICS CLINIC

Setting: 
Hospital.

Subjective:  
BJ is an 83-year-old community-dwelling woman who presented to the geriatrics clinic with a 2-day history of abdominal cramping and 8–10 loose, watery bowel movements each day. Three weeks ago she was treated for abdominal cellulitis with vancomycin and piperacillin/tazobactam ×2 days followed by clindamycin and levofloxacin to complete a 14-day course. Her last dose of antibiotics was 4 days ago.

Past Medical History:  
Insulin-dependent diabetes mellitus, rheumatoid arthritis, and hypertension.

Medications:  
Amlodipine 10 mg daily, prednisone 5 mg daily for arthritis, glipizide ER 5 mg daily, methotrexate 25 mg once weekly on Tuesdays, omeprazole 20 mg daily before breakfast, aspirin 81 mg daily.

Allergies:  
NKDA.

Social History:  
Lives alone with four children nearby for support.

Objective:  
Ht 5’4˝, Wt 158 lb, BP 127/57; P 95 BPM; RR 20; T 99.8°F.

Physical Examination:  
Within normal limits except for arthritic changes in digits, guarding, and tenderness on abdominal exam with healed wound/scar tissue on lower abdomen.

Labs/Radiology:  
Electrolytes within normal limits; BUN 26 mg/dL; serum creatinine 1.2 mg/dL, WBC 15.75 K/uL; stool specimen for C. diff. toxin positive.

Assessment:  
BJ is an 83-year-old woman on immune suppressant therapy and recent broad-spectrum antibiotic treatment who presents with abdominal tenderness and diarrhea consistent with C. diff. diarrhea. Dehydration with acute kidney injury is also present.

Plan:  
1. Begin metronidazole 500 mg every 8 hours for 14 days.
2. Adopt isolation precautions with gloves/gowns until diarrhea resolved. Strict handwashing protocol required.
3. Hold methotrexate and omeprazole for now.
4. Give 500 mL bolus of normal saline intravenously. Repeat basic metabolic panel tomorrow.
Rationale:

1. This patient has several risk factors for developing *C. diff.* diarrhea, including treatment with clindamycin, immunosuppressant therapy, advanced age, recent hospitalization, and potential use of a PPI. Although her infection is not within the median 2–3 days of antibiotic treatment, she does have exposure within the past 8 weeks, which is a risk factor. Metronidazole is the recommended antibiotic therapy for *C. diff.* diarrhea for initial cases unless the disease is life-threatening, which would require treatment with oral vancomycin. A 10- to 14-day course is suggested, and given this patient’s risk factors of immunosuppressant therapy and advanced age, the longer course is reasonable to select.

2. One of the most important aspects of *C. diff.* infection is the need to prevent spread of the organism and its spores to others. Strict handwashing and isolation procedures are recommended to accomplish this goal.

3. Immunosuppressant therapy increases the patient’s risk for developing a *C. diff.* infection and may inhibit rapid clearance from the body. Discontinuation of immunosuppressants is desirable; however, the long-term use of prednisone may have caused suppression of the hypothalamic-pituitary axis, and discontinuation of prednisone during an acute illness is not recommended. PPIs have been associated in some studies with increasing risk for *C. diff.* diarrhea; in addition, this patient has no current indication for use.

4. With an elevated serum creatinine and BUN coupled with the lower blood pressure and episodes of diarrhea, a bolus of normal saline to replace lost fluids is indicated to try and reverse the dehydration and acute kidney injury. Continued monitoring of electrolytes and renal function is important for a patient with several days of diarrhea and acute kidney injury.
Case 2: Nursing Home

Setting:
Nursing home.

Subjective:
RW is a 79-year-old resident of a nursing home who was identified by his son and niece as having poor oral intake and progressive weakness. He was admitted to the nursing home’s rehabilitation ward 7 months ago after suffering a stroke and did not require help for dressing, feeding, or ambulation when finished with his therapy. However, over the past 2 months he has lost 10 kg and is no longer able to ambulate without assistance. RW complains that food seems to stick in his throat, and he coughs after he drinks or eats more often than he used to. Two days ago he had worsening pain in his ankles and feet and was started on prednisone for a presumed gout attack.

Past Medical History:
Hypertension, gout, stroke, chronic kidney disease (baseline serum creatinine 1.5 mg/dL), and healthcare–associated aspiration pneumonia during previous hospitalization.

Medications:
Nifedipine extended release 60 mg daily, aspirin 81 mg daily, colchicine 0.6 mg daily, prednisone 20 mg daily ×5 days.

Allergies:
NKDA.

Social History:
Quit smoking in 2000, no history of alcohol or drug abuse.

Objective:
Ht 5’6”, Wt 128 lb; BP 120/62 mmHg; P 69 BPM; RR 18/min; T 97.1°F.

Physical Examination:
Frail-appearing elderly male; examination within normal limits except for dry mucous membranes, white patches on tongue and back of throat, bilateral lower extremity weakness, and reduced range of motion in ankles.

Labs:
Laboratory within normal limits except for sodium 134 mEq/dL, BUN 33 mg/dL, serum creatinine 1.6 mg/dL; INR 1.3.

Assessment:
RW is a 79-year-old male with weakness, weight loss, and oral thrush.

Plan:
1. Begin nystatin suspension swish and spit three times daily for 5 days.
2. Give medications with at least 4 oz of water.
3. Schedule for speech and physical therapy.
**Rationale:**

1. RW has complaints consistent with dysphagia, including food sticking in his throat and cough. In addition, he has dry mucous membranes and oral thrush, both associated with swallowing difficulties. For several months he has had a decrease in oral intake evidenced by weight loss, which will worsen with development of oral thrush. Oral thrush is a well-recognized contributor to dysphagia and requires treatment with nystatin or fluconazole. This patient is on a short course of prednisone for a flare of gout. Once the prednisone is discontinued, he will likely not need long-term treatment with nystatin.

2. When it becomes more difficult to swallow, patients are likely to take medications with a minimal amount of fluid, which may prevent their proper dissolution and absorption. In RW’s case the aspirin may lodge in the throat and cause discomfort.

3. RW has a history of stroke and aspiration pneumonia, increasing his risk for dysphagia. He may have recovered his ability to swallow in the first months after the stroke with speech therapy, but sometimes patients do not continue to adhere to speech therapy recommendations for swallowing techniques and exercises, and dysphagia may return. A re-evaluation (after treatment of oral thrush) could prove helpful in assessing his present abilities and identifying current exercises and techniques to improve his overall ability to swallow. In turn, this may allow him to increase fluid and protein consumption, reversing the downward trend in his activities of daily living.
### Clinical Pearls

- Older patients are frequently prescribed a PPI in the hospital for stress ulcer prophylaxis and inappropriately continued on the medication after discharge. Although a higher dose or chronic therapy may be indicated when the diagnosis of GERD is clearly established, the high prevalence of PPI continuation without true indication coupled with the possible risks of long-term use underscores the need to critically evaluate the appropriateness of the PPI when performing a drug regimen review.

- Although low-fat, low-sodium, or other restrictive diets are often an integral part of disease management, the clinical outcomes of such diets are less clear in frail or institutionalized elderly. Restrictive diets may not be recommended, despite a history of heart disease, diabetes, or other chronic diseases, among individuals with geriatric cachexia, swallowing problems, advanced dementia, palliative care directives, or in situations in which enjoyment of food is prioritized above disease management.

### Chapter Summary

Aging changes the physiology of the GI tract and the body's nutritional needs. Elderly patients are at increased risk for many GI problems such as GERD, nausea and vomiting, dysphagia, diverticular disease, constipation, fecal incontinence, and *C. diff.* diarrhea. In addition, oral health and nutritional status can deteriorate, increasing the risk for sarcopenia and frailty. The use of available pharmacotherapies for treating GI disorders in the older population differs in many respects from use in younger adults. Understanding the epidemiology of GI and nutritional disorders in older adults and their evidence-based management can help eliminate disparities in healthcare and promote quality of life and longevity for our aging population.

### Self-Assessment Questions

1. What physiologic changes related to aging increase the risk for GI disorders in older adults?
2. Why should complaints of dry mouth or altered taste sensation prompt a drug regimen review?
3. Which products are most likely to present a challenge when administering medications to an individual with dysphagia?
4. What are the important considerations when evaluating the presence of a PPI on the regimen of an elderly patient?
5. What are the most common causes of nausea among the elderly population?
6. What are the differences among anorexia, cachexia, and sarcopenia?
7. What medications cause constipation?
8. When is vancomycin a better choice for treating *C. diff.* infection than metronidazole?
9. What is the most common reason an older person develops fecal incontinence?
10. Which antibiotics are best for treating diverticulitis?

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Learning Objectives

1. Compare the prevalence of dementia across different age groups.
2. Contrast the different etiologies, symptoms, and therapies for mild cognitive impairment, Alzheimer disease (AD), vascular dementia, dementia with Lewy bodies, and frontotemporal dementia.
3. Develop a treatment plan for a patient with mild cognitive impairment or dementia.
4. Design a treatment plan for behavioral symptoms associated with dementia.
5. Distinguish the epidemiology and features of dementia and delirium in an elderly patient.
6. Devise a prevention and treatment plan for an elderly patient with delirium.
7. Recognize the impact of Parkinson disease (PD) and its treatment on the quality of life of patients and caregivers.
8. Recommend appropriate therapy for a senior individual with PD throughout the course of the disease.
9. Recommend nonpharmacologic and pharmacologic interventions for a person with PD experiencing depression and constipation.
10. Recognize the different etiologies and clinical presentation of seizures in the senior population versus the younger population with seizures.
11. Recommend appropriate therapy for a senior individual diagnosed with epilepsy, adjusting for pharmacokinetic and pharmacodynamic changes.
12. Recommend an appropriate titration schedule for a senior to switch antiepileptic drugs.
**Key Terms and Definitions**

**BETA AMYLOID:** Peptide of 39–43 amino acids formed after cleavage of the amyloid precursor protein. Beta-amyloid is insoluble in the brain and forms plaques associated with AD.

**CHEMICAL RESTRAINT:** Use of psychoactive medications as a matter of convenience in order to prevent a patient from moving about or to control behavior. No medical indication or safety issue, which would require treatment for the patient’s best interest, is present for use of a psychoactive medication to be considered inappropriate.

**DYSKINESIAS:** Uncontrollable, automatic, dance-like movements, commonly occurring when levodopa doses are peaking or “peak-dose dyskinesias.”

**EPILEPSY:** Chronic neurologic condition characterized by recurrent unprovoked seizures.

**HYPODERMOCLYSIS:** Infusion of isotonic fluids into the subcutaneous tissue. This avoids the potential safety issues of an intravenous infusion, therefore requiring less monitoring by nursing staff. However, the solution is limited to normal saline or 5% dextrose with 0.45% sodium chloride without additives.

**LEWY BODY:** Abnormal collection of proteins, usually alpha-synuclein, ubiquitin, and others, that forms inside nerve cells. In PD they are initially found in the substantia nigra, whereas in dementia with Lewy bodies (DLB) they are found in the hippocampus. However, as disease progresses, Lewy bodies will extend to many other parts of the brain, as observed at autopsy.

**MOTOR COMPLICATIONS:** Symptoms that include wearing off between doses and dyskinesias.

**MOTOR SYMPTOMS:** Collection of symptoms that commonly include tremor, bradykinesia, rigidity, and postural instability.

**NEUROLEPTIC SENSITIVITY:** Excess sensitivity to agents with dopamine effects, resulting in increased extrapyramidal effects. This is most often described as an attribute of patients with DLB seen when treated with antipsychotic agents.

**NEUROPSYCHIATRIC SYMPTOMS:** Noncognitive symptoms secondary to moderate-to-severe dementia, including psychosis, agitation, aggression, wandering, crying out, hostility, suspiciousness, anxiety, or depression.

**NONMOTOR SYMPTOMS/COMPLICATIONS:** Symptoms that commonly include swallowing difficulties, constipation and other gastrointestinal (GI) transit slowing, autonomic dysfunction, shuffling gait, masked facies, depression, dementia, anosmia, and others.

**OFF:** State in which medications are not working and the patient feels symptoms of PD.

**ON:** Symptom-free state, when PD medication is working.

**REFRACTORY EPILEPSY:** Although the definition is controversial, this term means the failure of two or more drugs and occurrence of one or more seizures per month over 18 months.

**WEARING OFF:** Sensation that the effects of medications for PD, typically levodopa, are diminishing; typically felt in between doses and occurring with increased frequency as PD progresses.
Introduction

The workings of the brain remain a mystery in many respects. Some elderly patients maintain a quick wit, enthusiasm for learning, and wisdom to share with the younger generations. Yet others are plagued with neurologic abnormalities that are not normal with aging. Dementia, delirium, PD, and epilepsy are more common in older adults, and their exact causes and cures are yet to be identified. This chapter reviews these neurologic conditions in the elderly patient, focusing on the optimal use of medications in this population.

Dementia

Etiology, Epidemiology, and Clinical Presentation Specific to Geriatrics

Dementia is a disease of the white matter of the brain, with various etiologies. It is defined by the Diagnostic and Statistical Manual of Mental Disorders, 5th edition (DSM-5) as cognitive decline in one or more domains (complex attention, executive function, learning and memory, language, perceptual-motor, or social cognition). In addition, the cognitive deficits must interfere with social or work activities for the diagnosis to be applied. Mild cognitive impairment (MCI) is a term used when the patient has memory or cognitive problems that do not qualify for the definition of dementia. From 10% to 16% of patients with MCI progress on to develop a diagnosis of dementia each year, with the remainder stable without clinically significant decline. Pharmacists may be the first to recognize that a patient may have MCI or dementia when problems with medication management are identified. Table 12-1 provides information related to the various subtypes of dementia and related disorders. Dementia is estimated to occur in 6% to 10% of individuals over 65 years of age; however, prevalence increases from 1% to 2% of the young-old (age 65–74 years) to 30% of those over 85 and crests at 58% of individuals older than 94.

When a patient presents with complaints of memory impairment, reversible causes should be identified and treated. These include hypothyroidism, depression, electrolyte disturbances, hepatic insufficiency, anemia, and vitamin B12 deficiency. In addition, if patient history indicates, serologic testing for neurosyphilis is performed. Many medications can cloud mentation as part of their pharmacologic effect. The most commonly associated medications are benzodiazepines, medications with anticholinergic properties, opioid analgesics, and anticonvulsants; however, amiodarone, digoxin, corticosteroids, nonsteroidal anti-inflammatory drugs, H₂ blockers, and many other medications have been reported to cause delirium. Dosage reduction or drug discontinuation is desirable to eliminate iatrogenic memory loss.

Vitamin B12 deficiency is associated with increasing age, atrophic gastritis, and acid-suppression therapy. Anemia may occur with vitamin B12 deficiency, but this effect may be masked with the current level of folic acid supplementation in cereals and breads consumed in the United States. The typically normal range (150–900 pg/mL) for vitamin B12 serum concentrations, also named cobalamin, is not a good marker of tissue vitamin B12 levels; measurement of folic acid and methylmalonic acid are required to clearly document vitamin B12 deficiency when vitamin B12 serum concentrations are in the low-normal range. In many cases it is easier and less expensive to replace vitamin B12 in individuals to bring serum concentrations above 300–500 pg/mL.

KEY POINT: Reversible causes of memory loss must be addressed, including medication-related issues, before a diagnosis of dementia can be applied.
Table 12-1. Some Diseases of Cognition

<table>
<thead>
<tr>
<th>Disease</th>
<th>Prevalence</th>
<th>Characteristics</th>
<th>Risk Factors</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mild cognitive impairment</td>
<td>5.4 million U.S. citizens (10% to 22% of older adults), 12% progress to dementia annually, 8% mortality rate</td>
<td>Varied, including prodromal AD, medical conditions, vascular disease, depression, or neurologic conditions</td>
<td>Age, Low educational attainment</td>
</tr>
<tr>
<td>AD</td>
<td>2.5–5.1 million U.S. citizens (10% of individuals older than 71), 70% of dementias</td>
<td>Early symptoms include difficulty remembering names and recent events, apathy and depression; later symptoms of impaired judgment, confusion and behavior change</td>
<td>Age, APO ε-4 alleles</td>
</tr>
<tr>
<td>Vascular dementia</td>
<td>2.4% of individuals older than 71, 17% of dementias</td>
<td>Symptoms overlap with AD, but progression occurs in a stairstep fashion with lower plateaus of functional impairment and focal neurological deficits</td>
<td>Hypertension, Diabetes, Age, Atherosclerosis, Male sex, Atrial fibrillation, Myocardial infarction, Heart disease, Smoking, History of stroke</td>
</tr>
<tr>
<td>DLB</td>
<td>15% to 20% of dementias, 0.7% of individuals older than 65</td>
<td>Symptoms overlap with AD, but alertness and cognition fluctuate day to day; visual hallucinations, muscle rigidity and tremors occur</td>
<td>Duplicate or triplicate copies of α-synuclein gene (familial cases only)</td>
</tr>
<tr>
<td>FTD</td>
<td>5% to 10% of dementias</td>
<td>Personality and behavior changes, difficulty with language and self-care, onset at younger age (average 58 years old), rarely occurs after age 75</td>
<td>Family history, Tau protein genetic mutation</td>
</tr>
<tr>
<td>Creutzfeldt-Jakob disease</td>
<td>1 case per million per year worldwide, increased 30–100 fold where familial cases cluster</td>
<td>Rapidly progressive memory impairment, incoordination, and behavior changes; mortality within 1–2 years</td>
<td>Prion protein gene on chromosome 20 (familial cases), Medical history of psychosis, Multiple surgeries, Live 10+ years on a farm</td>
</tr>
<tr>
<td>Normal pressure hydrocephalus</td>
<td>2–20 cases per million per year worldwide</td>
<td>Symptoms include memory loss, difficulty walking, and incontinence</td>
<td></td>
</tr>
<tr>
<td>Dementia of advanced PD</td>
<td>In later stages of PD, dementia may develop</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

AD, Alzheimer Disease; APO, Apolipoprotein; DLB, dementia with Lewy bodies; FTD, frontotemporal dementia; PD, Parkinson Disease.

Source: Compiled from references 2, 11, 126, and 127.
Alzheimer Disease

AD is the most common type of dementia, occurring in 60% to 80% of dementia diagnoses. Definite risk factors identified for AD are age, family history, head trauma, identified apolipoprotein e-4 mutations/polymorphisms, and Down syndrome. Early-onset cases of AD are usually attributed to inherited genetic mutations, or in the case of Down syndrome, an additional copy of chromosome 21. Late-onset AD is associated with polymorphism of the apolipoprotein e-4. Protective factors, such as increased educational attainment or dietary antioxidant consumption, may exist but have yet to be proved.

Multiple pathophysiologic theories are proposed and guide investigational drug development in AD. The cholinergic hypothesis involves the loss of cholinergic neuronal activity in the hippocampus and cortex. Currently available drug therapy with cholinesterase inhibitors (CIs) supports this hypothesis. Another hypothesis is the beta-amyloid hypothesis, which has developed because the location of beta-amyloid plaques, one of the hallmark features of AD at autopsy, corresponds to cognitive deficits. Tau proteins become hyperphosphorylated, producing neurofibrillary tangles. Cytokines and inflammatory mediators are elevated in the brains of individuals with AD, giving rise to the inflammation hypothesis. It is based on evidence that neuronal injury gives rise to interleukin-1 production, which in turn triggers a host of immune-mediated responses and beta-amyloid protein deposition. Other current theories consider mitochondrial function, glucose metabolism, and brain injury.6

A definitive diagnosis of AD is only given with autopsy, where beta-amyloid plaques and neurofibrillary tangles are found in the brain. More useful in practice are the National Institute of Neurologic and Communicative Disorders–developed criteria for clinical diagnosis of probable AD:

- Core features: presence of significant episodic memory impairment that is gradual and progressive, confirmed with objective neuropsychological testing
- Supportive features:
  - Presence of medial temporal lobe atrophy on magnetic resonance imaging (MRI)
  - Abnormal cerebrospinal fluid biomarkers (low amyloid beta 1-42, high tau or phosphor-tau concentrations)
  - Reduced glucose metabolism on functional positron emission tomography (PET) neuroimaging
  - Proven autosomal dominant AD mutation
- Exclusion of:
  - Other medical disorders, which account for these symptoms
  - A history of sudden onset, early occurrence of gait disturbances, seizures, or behavioral changes
  - Focal neurological features or early extrapyramidal signs7

The newer objective measures listed as supportive features are being evaluated primarily for research. The hope is that these objective biomarkers will test positive early on in the disease process, allowing for the use of effective interventions for prevention or cure while the disease is in a preclinical stage.8

Frequently, a patient may have symptoms of AD for several years prior to diagnosis, but family, co-workers, and friends begin to take on duties and responsibilities that the patient can no longer handle. For example, the spouse may take over paying bills and balancing the checkbook if the patient starts to make mistakes or forgets to pay bills on time. The timeline after diagnosis varies, but survival can range from 3 to 20 years, with a median of 4.2 years for men and 5.7 years for women.9 Some patients have a rapid decline, losing 5 points or more on the Mini-Mental State Examination (MMSE) each year, while others lose fewer than 2 points per year. Whatever the initial progression rate, patients tend to continue with that rate throughout the course of the disease. AD is the fifth leading cause of death in the United
States, and the disease is probably a significant contributor to deaths attributed to pneumonia, sepsis, and trauma.

**Vascular Dementia or Vascular Cognitive Impairment**

Multiple names are applied to cognitive impairment related to vascular disease in the brain, including vascular dementia, multi-infarct dementia, Binswanger disease, lacunar state, or vascular cognitive impairment. Vascular dementia is diagnosed when new-onset dementia occurs within 3 months of a cerebrovascular accident. In many cases, the course of vascular dementia follows a stair-step decline, with specific cognitive or functional deficits occurring that place the patient on a lower plateau. However, silent infarctions may occur and build until cognitive impairment is the first symptom of disease. Because the location and amount of tissue damage influence the cognitive deficits, patients with vascular dementia have differing clinical presentations. Small cerebrovascular infarcts less than 15 mm, called lacunar infarcts, may or may not precipitate cognitive changes, depending on where they occur in the brain. AD can coexist with vascular dementia as 77% of brain autopsies meeting criteria for vascular dementia also had AD in the Florida Brain Bank study. The pathology of vascular dementia involves evidence of cerebrovascular disease and infarction in the white matter of the brain. Diagnosis is frequently supported with MRI or computed tomography (CT) scan, which shows infarction coupled with evaluation of vascular risk factors. Risk factors for vascular dementia mirror those for stroke, heart disease, and atherosclerosis.

**Dementia with Lewy Bodies**

DLB was originally felt to be a rare disease, but with newer staining techniques for recognition of cortical Lewy bodies (at autopsy) it is now known to be the second or third most common type of dementia, depending on the study. It usually occurs in patients aged 75–80 years and has many overlapping features with AD. In addition to dementia, to be diagnosed with DLB the patient must have at least two of three features:

1. Fluctuating cognition with pronounced variations in attention and alertness
2. Recurrent detailed visual hallucinations
3. Spontaneous features of parkinsonism

To differentiate DLB from dementia of advanced PD, the timing of dementia and parkinsonian symptoms must be considered. In DLB, the onset of dementia should occur concurrently with the onset of parkinsonism (within 12 months), whereas in dementia of advanced PD the dementia occurs late in the course after PD has been well established in the individual.

**Neuroleptic sensitivity** is a secondary feature that is suggestive of DLB and particularly important in considering drug therapy, because antipsychotic therapy may be considered for a patient with visual hallucinations. Excessive sensitivity to D2 receptor blocking agents is seen and causes an increased morbidity and mortality in about half of patients with DLB treated with these agents. Patients with DLB exposed to neuroleptics had significantly more sedation, confusion, rigidity, and immobility. Mortality in one retrospective study was 2.7 times that of control patients. The atypical antipsychotics have been tried as an alternative, with mixed results. Case reports indicate enhanced sensitivity to adverse effects with clozapine, risperidone, olanzapine, and quetiapine, although some small studies indicate a modest therapeutic response to olanzapine and quetiapine. Small doses and close monitoring are indicated if an atypical antipsychotic is prescribed for a patient with DLB. In many cases, clinicians can educate caregivers and patients that hallucinations can remain untreated as long as they do not cause unnecessary fear or safety concerns, thereby preventing exposure to antipsychotic agents in a patient with DLB.
KEY POINT: Sensitivity to dopamine antagonists in patients with DLB occurs within 2 weeks of initiation or dose increase.

Frontotemporal Dementia

Frontotemporal dementia (FTD) is supported by atrophy of the prefrontal or anterior temporal areas of the brain on MRI. Patients will present with a decline in interpersonal conduct, with socially inappropriate behaviors such as rude, caustic, or sexually explicit remarks; loss of empathy and emotional blunting; and decline in personal hygiene. FTD has several subsets, including a behavioral variant (Pick disease) where behavior is a primary component and memory is initially well maintained, semantic aphasia where the meaning of familiar words is lost but other memory unaffected, and progressive aphasia, which is diagnosed when a patient presents with nonfluent spontaneous speech. Patients who are early in progressive or semantic aphasia will preserve social skills, but these break down similar to behavioral variant FTD at later disease stages as they progress to mutism. The incidence of FTD is highest in the youngest old, with usual onset occurring before age 60, and the prevalence does not increase in the higher age groups, as FTD often has a rapid progression.15

Other Types of Dementia

Normal pressure hydrocephalus is a reversible dementia caused by increased pressure in the ventricles of the brain, although on spinal tap the opening pressure is normal. Diagnosis is based on a classic triad of dementia, gait disturbance, and urinary incontinence. This etiology is important to identify because surgical placement of a ventriculoperitoneal shunt can potentially reverse the progression of the disorder.

Creutzfeldt-Jakob disease is a rare cause of dementia that develops over weeks to months, with rapid progression to death over 1–2 years. Characteristic findings on the electroencephalography (EEG) and in the cerebrospinal fluid (CSF) support it as a diagnosis, whether inherited or infectious in etiology. Neurosyphilis is another infectious cause of dementia. It occurs 10–20 years after a primary syphilis infection, manifesting as dementia, anxiety, paranoia, and mania. A positive reactive plasma reagin (RPR) or fluorescent treponemal antibody absorption (FTA-Abs) test indicate prior syphilis infection and raise the possibility of neurosyphilis in a patient with dementia. Positive testing of the CSF is required for definitive diagnosis. Because of its rare occurrence, current guidelines for dementia assessment do not recommend these tests in every patient presenting with dementia. However, if a patient presents with a new episode of psychosis along with dementia, screening with FTA-Abs followed with lumbar puncture is indicated in order to identify a potentially reversible cause of dementia.

Summary of Standard Treatment of Dementias

When MCI or dementia is diagnosed, comorbid conditions should be addressed early in the course of disease to limit their contribution to functional declines. Elimination of unnecessary medications should occur first, especially those with any anticholinergic or benzodiazepine properties. Retrospective studies have shown an increase in progression of dementia when patients with AD receive anticholinergic medications. In addition, the patient should be assessed for depression and treated if it is present. Depression causes apathy and difficulty with concentration, which can augment cognitive impairment.

KEY POINT: Up to one-third of patients with AD will have concurrent depression, and patients with depression may present with memory loss. These overlaps complicate the clinical picture.

Cardiovascular risk factors should be addressed, particularly for patients with AD or vascular dementia, as several observational studies indicate a more rapid decline may occur...
when hypertension, hyperlipidemia, or diabetes are not controlled. Vision and hearing should be assessed to ensure that communication can be optimized for as long as possible. Finally, exercise programs for both physical and cognitive activities are recommended.

Social issues should be tackled with family, friends, and caregivers. Patients should be encouraged to prepare advanced care directives and durable power of attorney documents. Wishes for long-term care may be discussed, as the disease course is expected to reduce the patient’s functional abilities over time until he or she will require 24-hour care, 7 days a week.

Currently, the mainstays of pharmacotherapy for dementia are the CIs and memantine, an NMDA receptor antagonist. Tacrine was the first CI on the market in the United States, but because of the risk for hepatotoxicity, it is no longer used. The pharmacokinetic comparisons of other agents are shown in Table 12-2. These agents have a Food and Drug Administration (FDA)–labeled indication for treatment of AD but are frequently used off-label for other types of dementia, some with evidence and some without.

AD is the most studied of the dementias, and current treatment algorithms from the American College of Physicians and the American Academy of Family Physicians distinguish a pathway for patients with mild-to-moderate as compared to moderate-to-severe AD. For mild-to-moderate AD, first-line therapy is a CI, to be titrated to the maximally tolerated dose in the therapeutic range (see Table 12-3). No clinical data place one CI above the other as an initial choice. If ineffective or not tolerated, a switch to another CI is suggested. If poor clinical response is noted, addition or substitution of memantine in patients with moderate AD is the next

Table 12-2. Pharmacology of Medications for Alzheimer Disease

<table>
<thead>
<tr>
<th>Generic Drug (Trade Name)</th>
<th>Mechanism of Action</th>
<th>Serum Half-life</th>
<th>Protein Binding</th>
<th>Food Delays Absorption</th>
<th>Metabolism</th>
<th>Renal Elimination</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Cholinesterase Inhibitors</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Donepezil (Aricept)</td>
<td>Reversible and noncompetitive inhibition of acetylcholine (ACH)</td>
<td>70–80 hours</td>
<td>96%</td>
<td>No</td>
<td>CYP2D6, 3A4</td>
<td>17% as unchanged drug</td>
</tr>
<tr>
<td>Galantamine (Razadyne)</td>
<td>Reversible and competitive inhibition of ACH; modulates nicotinic acetylcholine receptors</td>
<td>5–7 hours</td>
<td>10% to 20%</td>
<td>Yes</td>
<td>CYP2D6, 3A4</td>
<td>20% to 32% as unchanged drug</td>
</tr>
<tr>
<td>Rivastigmine (Exelon)</td>
<td>Reversible inhibition of both acetyl- and butyrylcholinesterases</td>
<td>2 hours (oral) 3 hours (patch)</td>
<td>40%</td>
<td>Yes (oral)</td>
<td>Hydrolysis in brain, D-methylation or sulfation in liver</td>
<td>Insignificant</td>
</tr>
<tr>
<td><strong>NMDA Receptor Antagonist</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Memantine (Namenda)</td>
<td>Prevents overstimulation of glutamate receptors to prevent excitotoxicity of neurons</td>
<td>60–80 hours</td>
<td>45%</td>
<td>No</td>
<td>Glucuronidation, reduction, hydrolysis</td>
<td>52% to 80% as unchanged drug</td>
</tr>
</tbody>
</table>

See reference 128 for additional information.
step. In moderate-to-severe AD, the pathway allows for a CI or memantine first-line, followed by combination therapy. Intolerance or loss of clinical benefit is addressed by switching from one CI to another, just as in the mild-to-moderate pathway. If there is a treatment failure, loss of benefit or intolerance after all three CIs and memantine have been tried, withdrawal of either or both medications is recommended for both algorithms. In essence, the current pathways are equivalent except that memantine can be tried first-line as monotherapy or as dual therapy with a CI in moderate-to-severe disease.\(^{17}\)

Also marketed is caprylidene, a medium-chain triglyceride that the body metabolizes to ketone bodies. It is classified as a medical food for AD. The potential mechanism of action is based on the fact that the brain may have impaired glucose metabolism and is better able to utilize ketone bodies for energy. While short-term results support its use, measures became nonsignificant at 12 weeks. Adverse effects include diarrhea, flatulence, dyspepsia, dizziness, and headache.\(^{18}\) It is rarely used in practice.

### Monitoring of Therapy

Monitoring for effectiveness of both CIs and memantine involves assessment from the patient, caregiver, and physician. Generally, effectiveness can be assessed after treatment for 3 months using standard instruments such as the MMSE, Clinician’s Interview-Based Impression of Change-Plus Caregiver Input, Activities of Daily Living, and/or the Neuropsychiatric Inventory Questionnaire, as described in Chapter 4.\(^{17}\)

Most commonly, CIs cause GI adverse effects including nausea, vomiting, diarrhea, and anorexia in 5% to 20% of patients due to

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**Table 12-3. Initiation and Titration of Drugs Used in Dementia**

<table>
<thead>
<tr>
<th>Drug</th>
<th>Initial Dose</th>
<th>Titration Schedule Every</th>
<th>Recommended Dose</th>
<th>Minimum Therapeutic Dose</th>
<th>Renal Adjustment</th>
<th>Formulations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Donepezil</td>
<td>5 mg/day</td>
<td>4 weeks</td>
<td>10 mg/day</td>
<td>5 mg/day</td>
<td>No</td>
<td>5- and 10-mg tablets; 5- and 10-mg orally disintegrating tablets; 23-mg film-coated tablet</td>
</tr>
<tr>
<td>Galantamine IR</td>
<td>4 mg 2×/day</td>
<td>4 weeks</td>
<td>8–12 mg 2×/day</td>
<td>8 mg 2×/day</td>
<td>Yes</td>
<td>4-, 8-, and 12-mg tablets; 4 mg/mL solution</td>
</tr>
<tr>
<td>Galantamine ER</td>
<td>8 mg/day</td>
<td>4 weeks</td>
<td>24 mg/day</td>
<td>16 mg/day</td>
<td>Yes</td>
<td>8-, 12-, and 24-mg capsules</td>
</tr>
<tr>
<td>Rivastigmine</td>
<td>1.5 mg 2×/day</td>
<td>4 weeks</td>
<td>6 mg 2×/day</td>
<td>3 mg 2×/day</td>
<td>No</td>
<td>1.5-, 3-, 4.5-, and 6-mg capsules; 2 mg/mL solution</td>
</tr>
<tr>
<td>Rivastigmine transdermal</td>
<td>4.6 mg/day</td>
<td>4 weeks</td>
<td>9.5–13.3 mg/day</td>
<td>9.5 mg/day</td>
<td>No</td>
<td>4.6-, 9.5-, and 13.3-mg patches</td>
</tr>
<tr>
<td>Memantine IR</td>
<td>5 mg/day</td>
<td>1 week</td>
<td>10 mg 2×/day</td>
<td>10 mg/day</td>
<td>Yes</td>
<td>5- and 10-mg tablets; 2-mg/mL solution</td>
</tr>
<tr>
<td>Memantine XR</td>
<td>7 mg/day</td>
<td>1 week</td>
<td>28 mg/day</td>
<td>28 mg/day</td>
<td>Yes</td>
<td>7-, 14-, 21-, and 28-mg capsules</td>
</tr>
</tbody>
</table>

See reference 128 for additional information.
the increased peripheral cholinergic stimulation. This pharmacologic effect can also cause incontinence and bradycardia. Dizziness and insomnia have been reported frequently. Once-daily CIs are generally started at bedtime, to reduce patient complaints of GI side effects; however, if insomnia occurs, doses can be given in the morning. If more than 2–3 days therapy of a CI is missed, the drug should be retitrated from the initial dose, to avoid increased adverse effects. The Beers criteria list CIs as contraindicated in patients with syncope. In one observational study, patients on CIs were hospitalized for syncope almost twice as often as patients with dementia not receiving a CI. Additionally, there was an increase in bradycardia, pacemaker placement, and risk for hip fracture.

Memantine is generally well tolerated with dizziness, headache, constipation, and somnolence reported more frequently than in placebo-treated subjects. Other reported adverse effects, such as agitation, falls, and accidental injuries, did not occur more often in the memantine-treated patients, although they were important issues in this patient group.

Pharmacotherapy of Other Dementias

Less is known about optimal pharmacotherapy of other dementias. Generally, the medications used to treat AD may be tried, and patients are assessed for clinical response within a similar timeframe as with AD. One exception is FTD, which rarely responds to CIs. In fact, one study indicates these agents may aggravate behavioral problems in FTD patients.

Review of Evidence Base Supporting Treatment Recommendations for Elderly Patients

As dementia is a syndrome found primarily in older adults, all studies have included geriatric patients. Several reviews and meta-analyses have been published to summarize the evidence for effectiveness and safety of the CIs and memantine in treatment of dementia and MCI. For AD, effectiveness data agree across most studies and all meta-analyses that cognition, function, and behavior are improved with CIs, although debate continues as to whether the statistical significance translates to clinically important differences. At least 26 well-controlled studies of CIs in AD were evaluated by one author, and 59 studies including over 16,000 subjects in CIs and/or memantine for dementia or MCI by another. The beneficial effect is modest at best, and a subgroup of individuals appears to have clinical benefit. Similar conclusions were drawn in the evidence review that included AD along with other dementias, although the numbers of subjects were much smaller in the non-AD studies. Although some pharmacologic differences are seen in the CIs, no clinical differences are seen with therapeutic or adverse effects when the agents are compared; therefore, no currently available CI is preferred for initial treatment over another.

A higher dose of donepezil was approved for individuals with AD who do not receive adequate response from lower doses of the CIs after at least 3 months of treatment. The 23-mg tablet is film-coated with a time to peak at 8 hours instead of 3–4 hours. However, controversy exists as to the risk-benefit ratio of the higher dose. Subjects receiving donepezil 23 mg experienced nearly a two- to threefold higher frequency of adverse events, with 30% of patients discontinuing treatment early. Small statistical improvement was shown in cognition, but global benefit was not shown except in subgroup analysis of U.S. subjects. A U.S. consumer advocacy group has called for removal of the 23-mg tablet from the market.

Similarly, evidence for the effectiveness of memantine in dementia shows statistically significant improvement in cognition, function, and reduction in caregiver burden, although clinical significance is not as clear. Withdrawal rates are similar for both treatment and placebo groups, at 7% to 13%. Evidence supports use in moderate-to-severe AD; however, no benefit has been shown in patients with mild disease. Information published on use of memantine in DLB report mixed results. In one report, delusions, halluci-
nations, agitation, and parkinsonism worsened in some patients. However, in another report DLB hallucinations emerged with memantine dechallenge and resolved with memantine rechallenge. Randomized, controlled trials have been small and tended to include both patients with DLB and patients with dementia of advanced PD, making it difficult to draw conclusions.

The combination of a CI and memantine is recommended in clinical practice guidelines for moderate-to-severe AD and is frequently tried for patients who continue to deteriorate. Few studies have been done with the combination; donepezil in combination with memantine has shown statistically significant improvements in measures designed for severe dementia assessment. A trial that allowed any CI for maintenance did not show significant change when memantine was added.

Three randomized, controlled trials evaluated over 3,500 subjects with MCI for the effect of CIs on progression to dementia. Dropout rates were high, 40% in treatment groups and 29% in placebo groups, but the risk for progression to dementia or AD was reduced 25% in treated subjects compared to control subjects. One study noted this positive effect to occur predominantly in subjects who were carriers of the apolipoprotein ε-4 genotype.

Only one controlled study with a CI in DLB has been performed and indicates benefit with reduction of apathy, anxiety, delusions, and hallucinations. Open-label studies of the use of CIs and memantine in FTD show no benefit or worsening of disease. Small controlled trials of certain selective serotonin reuptake inhibitors (SSRIs) to reduce certain behaviors are promising.

**Common Problems Encountered When Treating Elderly Patients**

**Neuropsychiatric Symptoms**

Although cognitive decline is the hallmark feature of dementia, neuropsychiatric (NP) symptoms typically cause the most anxiety and stress for patients and caregivers. They include delusions, hallucinations, repetitive activities, sleep disturbances, and mood changes. These symptoms are frequently called behavior problems in that they precipitate agitation, physical aggression, psychosis, and wandering—behaviors that cause problems with caregiving. However, the better term refers to them as symptoms rather than problems because they frequently result from an undiagnosed underlying issue, which the patient with dementia cannot communicate effectively to caregivers in order to achieve a resolution.

NP symptoms generally manifest as the disease progresses into a moderate-to-severe stage when the patient is partially functional but has begun to lose the ability to perceive and communicate effectively. Nursing home admission becomes likely as caregivers are unable to provide the amount of care needed. When the dementia progresses to the end stage, the patient’s functional status will have diminished such that he or she is unable to interact with others or the environment and becomes bedbound. NP symptoms are no longer discernible.

When new NP symptoms develop, the first step is to assess the patient for a medical or environmental precipitant that can be corrected. For example, a patient with moderate-stage AD who starts wandering at night should be evaluated for changes in caffeine intake, new medications, excess heat in the bedroom, or strange noises at night. Any of these items could cause the patient to have sleep problems that he or she could not communicate effectively to caregivers. Pain is a common medical precipitant to NP symptoms and should always be considered.

Evidence supports the use of nonpharmacologic treatments for NP symptoms, although the treatments are widely varied. Person-centered bathing, where the patient was kept covered at all times during the bath, showed significant reduction in agitation compared to standard bathing procedures. Use of lavender oil, lemon balm, and pet and music therapy has likewise shown reduction in agitation. Exercise training coupled with caregiver education reduced
depression and improved functional status in a randomized controlled trial.9,29

Medications are frequently used when nonpharmacologic interventions fail or are impractical. Generally, a patient should be evaluated to determine whether only acute, as-needed medication is required or chronic/maintenance treatments are necessary. Benzodiazepines and antipsychotics are most commonly used when acute rescue medication is needed, and CIs, memantine, SSRIs, or atypical antipsychotic agents are more often prescribed for maintenance medications, as described below.

CIs and/or memantine may be tried if the patient is not already being treated with these agents. However, evidence to support their effectiveness is meager. In DLB, it is especially useful to try CIs first, as increased sensitivity to adverse effects of other agents is likely. Certain SSRIs may be effective if anxiety is present, although it may be difficult to objectively assess the presence of anxiety, making assessment of their benefit challenging. However, withdrawal of any psychoactive may be attempted after 3–6 months, as these symptoms do not consistently persist as the disease progresses. Valproic acid at a dose of 125–500 mg daily may be tried for symptoms of agitation and aggression, sleep-wake disruption, and disinhibition (manic-like behaviors), although evidence of effectiveness is also sparse.

Antipsychotics are frequently the drugs of choice for psychosis, psychomotor agitation, and aggression in patients with dementia. Evidence of effectiveness is not strong, and concerns over an increased risk for mortality in elderly patients with dementia when these medications are used have forced manufacturers to include a boxed warning on both typical and atypical antipsychotics. A multicenter randomized controlled clinical trial compared risperidone, olanzapine, and quetiapine to placebo in treatment of psychosis, aggression, and agitation in nursing home residents with AD. The primary outcome of interest was time until discontinuation of treatment for either lack of effectiveness or adverse effects. No difference was seen with discontinuation occurring from 5–8 weeks after initiation of the antipsychotic or placebo, although the reason for discontinuation was lack of effectiveness for the placebo group compared to presence of significant adverse events in the antipsychotic groups. Improvement was seen in 21% of placebo-treated subjects and 26% to 32% of antipsychotic-treated subjects.30

The Agency for Healthcare Research and Quality has published a summary on the use of atypical antipsychotic agents for off-label indications. It states that although atypical antipsychotics improve behavioral symptoms of dementia, effect sizes are small and adverse effects are significant. It lists the risk of death at 1 for every 100 patients treated. In addition, risperidone and olanzapine are noted to increase the risk of stroke.31 Quality improvement initiatives aimed at reducing the use of antipsychotics in nursing home patients have been implemented by the Centers for Medicare & Medicaid Services, resulting in the national prevalence rate dropping from 23.8% to 10.2%.32 Continued efforts are needed to ensure antipsychotic use is limited to patients in whom the benefits clearly outweigh the risks, appropriate monitoring with a validated tool occurs, and periodic dose reductions are attempted.

**Delirium**

**Etiology, Epidemiology, and Clinical Presentation Specific to Geriatrics**

**Definition**

Delirium can be confused with dementia because both disorders are characterized by altered cognition and memory impairment. The patient with delirium may develop confusion, distractibility, disorientation, disordered thinking, hallucinations, and agitation all within hours or days. The hyperactive, agitated subtype of delirium is most recognized and concerning to the clinician,
as frequently the patient is pulling out catheters, intravenous lines, or other tubes and may be a danger to him- or herself or others. However, patients experiencing a hypoactive delirium are subdued and quiet, unable to interact with their surroundings. A third type of delirium is mixed, with the patient switching between hyperactive and hypoactive states.33

The DSM-5 states that delirium is a disturbance in attention and awareness, developing over hours to days, with fluctuation over the course of the day. In delirium, the patient has a reduced ability to focus or shift attention and is unaware of the environment. Memory impairment and disorientation are identified when the patient is questioned. Sensory impairment is also seen, as the patient may confuse loud noises with gunshots, misinterpret television programs as a party occurring in the room, or have the inability to interact appropriately with objects at the bedside.1

Delirium has a highly variable course. Studies indicate from 20% to 69% of patients recover from delirium within 1 day; however, as many as 15% may have symptoms lasting 10 days or more.34 Individuals with advanced age or pre-existing dementia are likely to have a more prolonged course, as will those with multiple contributing causes. Therefore, delirium is considered a syndrome of the elderly.

Epidemiology and Pathophysiology

Delirium has been reported in 29% to 64% of hospitalized older adults, with an incidence as high as 82% of patients in intensive care.35 One study of postoperative patients identified delirium occurring within 7 days after surgery in 44% of subjects.36 Within the geriatric nursing home population, the overall occurrence of delirium is as high as 36%.33 Recognizing delirium is important, because it is associated with an increase in mortality at 30 days and 6 months, reportedly as high as 76% in one study. Morbidity is also higher in patients with delirium, evidenced by longer hospital stays, increased time in the intensive care unit, pneumonias, and pressure sores. Finally, costs increase when delirium is present.

Several pathophysiologic theories have been proposed; however, neurotransmitter disruption particularly of acetylcholine and dopamine are most supported. Inflammation, metabolic disorders, or electrolyte disturbances may also play major roles.35

Numerous risk factors for delirium have been identified. Many medical and surgical conditions can precipitate delirium, but increased age and the presence of dementia are clearly associated with an increase in the risk for delirium. Postoperative delirium increased from 22% for age 50–59 years to 92% in patients over 80.36 Individuals with pre-existing brain pathology lack sufficient cognitive reserve to balance a sudden alteration in neurotransmitters.

Medications have been implicated as a cause in 30% of delirium cases. Any medication that has central nervous system (CNS) effects can cause delirium and confusion, especially anticholinergic agents, analgesics, sedative/hypnotics, antimicrobial agents, muscle relaxants, corticosteroids, anticonvulsants, antidiabetic drugs, and GI agents. In addition, abrupt discontinuation of alcohol or depressant medications may cause delirium as part of the withdrawal syndrome.

Clinical Presentation

Delirium is frequently overlooked by clinicians, especially if the patient exhibits hypoactive symptoms. The criteria for diagnosis from the DSM-5 have been adapted into several screening tools. The Confusion Assessment Method is one simple tool that has been validated in multiple populations and can be applied by any health-care provider to identify the patient likely to have delirium (see Table 12-4).37 Generally, features are assessed by asking a series of questions to a family member, friend, or nurse who has spent time with the patient and knows the patient’s baseline cognitive status. For delirium to be present, the patient must have features 1 and 2 and either feature 3 or 4.
Fundamentals of Geriatric Pharmacotherapy

Delirium should be distinguished from dementia, as both of these may cause a patient to be unable to correctly answer questions about orientation; however, delirium has the contrasting features of inattention, acute onset, and fluctuation in alertness or consciousness. Patients with dementia will have a slow onset of symptoms and are alert. Because of the high mortality and morbidity attributed to delirium, any complaint from a family member or nurse that “the patient is not himself/herself” should be investigated in spite of the nonspecific nature of the observation.

Summary of Standard Treatment of Delirium

Preventive Strategies

Interventions have been proven to reduce the incidence of delirium in elderly hospitalized patients. In a multicomponent model for hospitalized elderly patients, delirium episodes occurred in 9.9% of the intervention group, compared to 15% of the control group.\textsuperscript{38} Interventions included an orientation protocol, cognitive stimulation, environment control, nonpharmacologic sleep aids, early mobilization, minimization of physical restraints, visual and hearing aids for those with impairment, dentures for those without teeth, other personal effects, and early volume repletion for patients with dehydration. This intervention has been successfully replicated in other institutions.\textsuperscript{39,40} Similar interventions can be adapted for use in nursing home and home care patients to reduce the risk of delirium. Volunteers may be recruited to provide added nonpharmacologic support when friends, family, or nursing staff are not available.

Recommended pharmacologic considerations to prevent delirium include continuation of medications that may cause withdrawal symptoms if abruptly stopped and avoiding medications with a high potential for causing delirium, if possible. Also, adequate pain management,
using nonopioid analgesics if possible or the lowest opioid dose possible, has been shown to reduce the incidence of delirium.\textsuperscript{41} Melatonin has been used successfully at low doses to help maintain the sleep-wake cycle.

**Treatment or Removal of Underlying Cause**

Early identification and treatment of delirium is expected to improve outcomes, but data to support this are lacking. However, not every case of delirium can be prevented. After delirium is identified, the first step is to conduct an assessment for the underlying cause(s). The history, physical examination, and basic laboratory testing to identify infection, myocardial infarction (MI), electrolyte abnormalities, pain, or a change in medications is necessary.\textsuperscript{33} Serum drug levels and/or a urine drug screen may provide valuable information. Medical or surgical treatment to correct the underlying cause is imperative for the patient to regain previous cognitive function.

**Supportive Measures**

Supportive measures should be instituted simultaneously with treatment of the underlying cause. Having a friend or family member present to reassure and redirect the patient can help avoid the need to apply restraints, which usually worsen delirium. In addition, patients may injure themselves as they attempt to get out of bed while in restraints. But if the patient is at risk for injuring him-or herself or others, restraints may be required. The redirection by a caregiver at the bedside distracts the patient from pulling out a parenteral line or catheter. It is useful to remind the patient of the time, and placement of a clock, calendar, and family pictures may help with this task. In communicating with the patient in delirium, it is best to use clear language, little medical terminology, a tranquil voice, and few abstractions.

The environment should be kept at a comfortable temperature, with controlled excesses of noise. A radio or television can be soothing if tuned into appropriate programming. Lighting should be adequate during the daytime, and a nightlight may be helpful. If the patient wears glasses, hearing aids, or dentures, have them in place as much as possible to reduce sensory deficits and possible misperceptions. Both overand understimulation should be avoided.

A nonpharmacologic approach to improving sleep in patients with insomnia may improve delirium. Use of warm drinks (noncaffeinated tea or milk), soothing music, and back massage have been used. Hospital or nursing home noises and interruptions should be minimized during the night to prevent waking patients.

Inadequate hydration was identified as a risk factor for delirium in nursing home residents. Frail elderly patients frequently reduce intake of nutrition and fluids in response to infection, pain, or other insult, quickly resulting in dehydration, given that elderly persons already have lower total body water compared to younger patients. Quick attention to providing maintenance fluids either orally, intravenously, or through hypodermoclysis may prevent severe dehydration and its related morbidity or risk for delirium.\textsuperscript{42}

**Pharmacologic Management**

When nonpharmacologic measures are in place and steps to address the underlying cause of delirium are implemented, the patient should be re-evaluated. If the behaviors associated with delirium are not problematic, no further therapy is necessary. However, in some cases agitation and combative behavior must be managed pharmacologically to prevent danger to the patient or others and to allow evaluation and treatment by the medical team. This should be a small minority of patients. Pharmacologic measures for delirium management can be considered chemical restraints when used to control behavior that is undesirable but innocuous, especially if administered for extended periods of time.

**Review of Evidence Base**

**Supporting Treatment Recommendations for Elderly Patients**

Little published data are available to guide the use of medications in this situation, and no medi-
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cations have FDA approval for use in delirium. A systematic review of antipsychotic medication in older surgical patients concluded that low-dose haloperidol, risperidone, or olanzapine administered prophylactically reduced the risk of delirium, but many of the included studies were of low quality and high bias. Small uncontrolled studies provide limited evidence that low-dose, short-term use of antipsychotics reduce severity of an established delirium by 43% to 70%. Given the lack of strong evidence and risk of adverse drug effects, antipsychotic agents are presently recommended only for patients with hyperactive delirium that poses a risk of harm to the patient or others. Doses recommended for elderly patients with delirium are significantly lower than for younger adults, as shown in Table 12-5. In an elderly patient, haloperidol 0.5–1 mg is the preferred drug and dose, to be used as needed. Patients should be re-evaluated no sooner than 30–60 minutes after the dose. The dose may be repeated after this time until the patient is manageable or until a maximum of haloperidol 5 mg is reached. The goal of treatment is not to convert a hyperactive delirium into the hypoactive form. If longer therapy is needed, atypical antipsychotic agents should be considered.

Benzodiazepines have been used as second-line treatment when antipsychotic agents were not effective. Again, their use in delirium is not well studied, and, as CNS depressants, they may worsen confusion and sedation. Furthermore, benzodiazepines are associated with increasing incidence of delirium. Lorazepam is most frequently used, as it is more water-soluble than other benzodiazepines, has an intermediate elimination half-life, and is available in oral, intramuscular, and intravenous formulations.

**Parkinson Disease**

*Etiology, Epidemiology, and Clinical Presentation*

PD affects approximately 1% of the population over the age of 60 and 4% to 5% over the age of 85. Next to AD, it is the second most common neurodegenerative disease.

The primary cause of PD is believed to be the depletion of the dopamine-producing neurons in the substantia nigra pars compacta. Symptoms of the disease are believed to become present when ~80% of these neurons have

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### Table 12-5. Antipsychotic Agents Used in Delirium with Older Adults

<table>
<thead>
<tr>
<th>Medication</th>
<th>Initial Recommended Dose</th>
<th>Maximum Daily Dose</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aripiprazole</td>
<td>5 mg po</td>
<td>15 mg</td>
<td>Case series and reports in young and older adults</td>
</tr>
<tr>
<td>Haloperidol</td>
<td>0.25–0.5 mg po or IV</td>
<td>2–5 mg</td>
<td>IV route is off-label and associated with QTc prolongation</td>
</tr>
<tr>
<td>Olanzapine</td>
<td>2.5–5 mg po</td>
<td>10 mg</td>
<td>Anticholinergic side effects</td>
</tr>
<tr>
<td>Quetiapine</td>
<td>12.5–25 mg po</td>
<td>150 mg</td>
<td>Postural hypotension</td>
</tr>
<tr>
<td>Risperidone</td>
<td>0.25–0.5 mg po</td>
<td>4 mg</td>
<td>EPS with higher doses</td>
</tr>
<tr>
<td>Ziprasidone</td>
<td>20 mg IM</td>
<td>100 mg</td>
<td>Case reports in young, critically ill patients; significant risk for dose-related QTc prolongation</td>
</tr>
</tbody>
</table>

EPS, extrapyramidal symptoms; IM, intramuscular; IV, intravenous; po, by mouth.
been destroyed. The decrease in dopamine is the primary target of symptomatic treatment, as currently there is no cure or disease-modifying therapy available. The disease is slowly progressive, which makes follow-up absolutely necessary.

Clinically, patients with PD present with one or more of the following motor symptoms: resting tremor, bradykinesia, stiffness, and postural instability. Typically, a person presents asymmetrically, with symptoms being worse or only present on one side of the body. As the disease progresses, there is bilateral involvement. There are also many nonmotor complications of the disease, which may be present at initial presentation or may occur as the disease progresses. The nonmotor symptoms include micrographia, a masked appearance of the face, anosmia, urinary incontinence, depression, dementia, orthostatic hypotension, constipation, sialorrhea, increased sweating and oily skin, as well as sexual dysfunction. These nonmotor symptoms will not occur in all patients, and complaints of these problems may occur at any point in the disease process. However, it is important to realize the significant impact these nonmotor symptoms have on quality of life. Patients with PD may even rate nonmotor symptoms as more bothersome than the motor symptoms of the disease.47 The initial presentation is no different in an elderly patient compared to a younger cohort; however, the reasons attributed to symptom presentation may be different. The stiffness and slowness experienced with PD may be attributed to other disease states in older adults, such as osteoarthritis. Elderly patients may present later in the disease course, as their ability to manipulate their daily routine may be easier, compared to a younger individual who may still be employed. Attributing symptoms of PD to “getting old” may be another reason elderly patients do not present as early in the disease course as younger patients.

KEY POINT: Elderly patients may attribute symptoms of PD, such as slowing of movement and rigidity, to other disease states or “getting old.”

As the disease progresses, motor complications may arise. These can include wearing off between doses and dyskinesias, which are involuntary, repetitive movements typically seen when a person with PD is in the “on,” or treated, state. Dyskinesias occur in approximately 40% of patients with PD at some point in their disease process.

PD has a significant impact on both the lives of patients affected with PD as well as their caregivers. People with PD lose their ability to function independently as the disease progresses, and early in the disease process they commonly lose their fine-motor skills. Also, approximately 50% of PD patients will experience depression.48

As the disease progresses and functional deficits increase, so does caregiver strain. The caregiver’s quality of life is typically impacted negatively as care demands increase.49 Some of the factors that can increase the risk of nursing home placement include impairment of function of the person with PD, decreased ability to complete activities of daily living (ADL), dementia, and hallucinations.50

Summary of Standard Treatment

The American Academy of Neurology (AAN) produces guidelines for the initially presenting patient, as well as the patient experiencing motor complications, which may occur as the disease progresses and dopaminergic therapy is continued.51,52 The gold standard of symptomatic treatment, levodopa/carbidopa, is an available option for treating the initially presenting patient (see Table 12-6). However, due to the risk of dyskinesias seen with long-term use of levodopa, clinicians will typically elect to delay starting levodopa in younger patients and utilize alternative agents as first-line therapy unless
Table 12-6. Drugs, Common Dosages, and Required Dose Adjustments

<table>
<thead>
<tr>
<th>Drug</th>
<th>Daily Dose (mg)</th>
<th>Mild-Moderate Renal Impairment</th>
<th>Moderate-Severe Renal Impairment</th>
<th>Hepatic Impairment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Levodopa</td>
<td>200–1,000+</td>
<td>No</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>Carbidopa</td>
<td>25–75</td>
<td>No</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>Amantadine</td>
<td>200–400</td>
<td>Yes</td>
<td>Yes</td>
<td>No</td>
</tr>
</tbody>
</table>

**Dopamine Agonists**

- Bromocriptine: 15–90 mg
  - Mild-Moderate Renal Impairment: No
  - Moderate-Severe Renal Impairment: No
  - Hepatic Impairment: Use with caution
- Pramipexole IR: 1.5–4.5 mg
  - Mild-Moderate Renal Impairment: Yes
  - Moderate-Severe Renal Impairment: Yes
  - Hepatic Impairment: No
- Pramipexole CR: 1.5–4.5 mg
  - Mild-Moderate Renal Impairment: Yes
  - Moderate-Severe Renal Impairment: Yes
  - Hepatic Impairment: No
- Ropinirole IR: 1.5–24 mg
  - Mild-Moderate Renal Impairment: No
  - Moderate-Severe Renal Impairment: Use with caution
  - Hepatic Impairment: Use with caution
- Ropinirole CR: 2–24 mg
  - Mild-Moderate Renal Impairment: No
  - Moderate-Severe Renal Impairment: Use with caution
  - Hepatic Impairment: Use with caution
- Rotigotine: 2–8 mg
  - Mild-Moderate Renal Impairment: No
  - Moderate-Severe Renal Impairment: No
  - Hepatic Impairment: No
- Apomorphine: 3–6 mg
  - Mild-Moderate Renal Impairment: Yes
  - Moderate-Severe Renal Impairment: Use with caution
  - Hepatic Impairment: Use with caution

**COMT Inhibitors**

- Entacapone: 400–1600 mg
  - Mild-Moderate Renal Impairment: No
  - Moderate-Severe Renal Impairment: No
  - Hepatic Impairment: Use with caution
- Tolcapone: 300–600 mg
  - Mild-Moderate Renal Impairment: No
  - Moderate-Severe Renal Impairment: Use with caution
  - Hepatic Impairment: Do not use

**MAO-B Inhibitors**

- Selegiline: 5–10 mg
  - Mild-Moderate Renal Impairment: No
  - Moderate-Severe Renal Impairment: No
  - Hepatic Impairment: No
- Selegiline ODT: 1.25–2.5 mg
  - Mild-Moderate Renal Impairment: No
  - Moderate-Severe Renal Impairment: No
  - Hepatic Impairment: No
- Rasagiline: 0.5–1 mg
  - Mild-Moderate Renal Impairment: No
  - Moderate-Severe Renal Impairment: Use with caution
  - Hepatic Impairment: Yes

**Anticholinergics**

- Benztropine: 0.5–4 mg
  - Mild-Moderate Renal Impairment: No
  - Moderate-Severe Renal Impairment: No
  - Hepatic Impairment: No
- Trihexyphenidyl: 1–6 mg
  - Mild-Moderate Renal Impairment: No
  - Moderate-Severe Renal Impairment: No
  - Hepatic Impairment: No

COMT, catechol-O-methyltransferase; MAO, monoamine oxidase.

*Not studied in this specific subset of patients.

See reference 128 for additional information.
symptoms of PD are overly bothersome and impact quality of life. Other initial options available for the patient with mildly bothersome symptoms include the monoamine oxidase type B inhibitors, selegiline and rasagiline, as well the dopamine agonists bromocriptine, pramipexole, ropinirole, and rotigotine.51 Selegiline has been shown to decrease the rate of decline in motor scores of the United Parkinson’s Disease Rating Scale,51,53,54 and rasagiline has shown improvement of the ADL and motor subscales.55 Dopamine agonists are typically not the first choice in those experiencing PD symptoms that are having a significant impact on function and quality of life. Practitioners typically employ levodopa/carbidopa in these patients.51,56,57

Over time, wearing off and dyskinesias are seen with long-term use of levodopa/carbidopa. The AAN offers guidance on managing these complications.52 The addition of entacapone or rasagiline are both level A evidence interventions in those individuals experiencing wearing off between doses of levodopa/carbidopa. The addition of ropinirole, pramipexole, or rotigotine is also an option in the patient experiencing wearing off. It is important to remember that the dose of levodopa should be empirically decreased, as add-on therapies can worsen dyskinesias by increasing the peak level of levodopa. Apomorphine has level C evidence for use in wearing off, and is used clinically for episodes of sudden “off” or freezing. Apomorphine, however, is only appropriate for as-needed use and should not be used as a scheduled medication unless freezing is occurring at consistent times. It also requires the scheduled dosing of an anti-emetic because of its tendency to cause extreme nausea. Although not supported by evidence, the practice of decreasing the dosing interval (increasing the number of daily doses) is also a viable option for wearing off. Changing from immediate-release to sustained-release levodopa/carbidopa for relief of wearing off is not supported by evidence and is not clinically effective for this problem.52

**KEY POINT:** Doses of levodopa/carbidopa should be empirically decreased when a dopamine agonist, catechol-O-methyltransferase inhibitor, or monoamine oxidase type B inhibitor is added to a regimen to decrease the incidence of peak-dose dyskinesias.

Dyskinesias, resulting from levodopa/carbidopa doses, can be extremely bothersome, and the addition of amantadine has level C evidence to support its use.52 Although evidence is not available to support the practice, decreasing the dose of levodopa/carbidopa and decreasing the dosing interval at the same time is used clinically to assuage dyskinesias.

Although there is currently no cure for PD, the search for disease-modifying or “neuroprotective” interventions draws much research interest. The DATATOP trial with selegiline and the ADAGIO trial with rasagiline failed to show a disease-modifying benefit of those drugs.58,59 The use of coenzyme Q10 has shown mixed results in several small trials, and a meta-analysis suggested amitriptyline may have the potential for disease modification60; however, nothing definitive has emerged. Obviously, the use of a tricyclic antidepressant is not a good choice in any elderly patient regardless of indication.

**Review of Evidence Supporting Treatment Recommendations in the Elderly**

On initial presentation, the clinician treating the elderly patient is faced with the challenge of balancing good symptom control and improved quality of life with the side effect burden of currently available treatment options. The clinician must also ensure drug interactions are avoided and make certain to not exacerbate other disease states with the therapy. These tenets continue to be important as the disease...
progresses and motor complications develop as well as when electing to treat the nonmotor symptoms responsive to drug therapy.

The AAN does not currently have a guideline for specifically treating the elderly patient with PD. However, keeping the patient’s concomitant diseases and agent characteristics in mind will help circumvent major problems in treatment.

Because of the increased incidence of the disease with age, virtually all clinical trials of agents for the treatment of PD have no maximum age at which individuals are excluded. However, most trials of agents include the common, broad, and loosely-defined exclusion criteria of individuals with severe systemic disease, dementia, depression, or other psychiatric illnesses. This prevents the inclusion of a more aged cohort into these trials, and the typical average age seen is between 60 and 65.

Currently, there are no clinical trials that specifically target the safety and efficacy of agents for elderly PD patients in a randomized fashion. A retrospective analysis of the dopamine agonists in a small cohort of patients 80 and older showed >50% of patients were unable to tolerate dopamine agonists or did not demonstrate efficacy with the use of the agents. Hallucinations were seen in 21% and 25% of patients receiving pramipexole and ropinirole, respectively. Orthostasis was also seen in 5% to 6% of patients receiving a nonergot alkaloid dopamine agonist. A retrospective analysis of rotigotine trials showed those 75 and older with early PD were more likely to experience nausea and dizziness compared to those under age 75. And, in the same analysis, those with advanced PD aged 75 and older were more likely to experience nausea and falls compared to the under-75 cohort. A few post hoc analyses of rasagiline showed those older than 70 were no more likely to experience adverse effects with the drug compared to younger patients and experienced similar efficacy.

Common Problems Encountered in the Senior Population with Parkinson Disease

Agent-Related

Levodopa/carbidopa will likely become part of any PD regimen at some point during the disease course, and in geriatric individuals many times will be the starting point of therapy. Individuals taking levodopa/carbidopa typically commence with three times daily dosing. However, as the disease progresses this dosing interval typically decreases, with some patients taking greater than eight doses of levodopa/carbidopa per day. This can be difficult for patients to manage, especially in those with other concomitant disease states for which medications are taken. The ability to adhere to such a regimen should always be considered. Levodopa/carbidopa is also a medication for which timely medication administration is important, and for those patients residing in long-term care facilities, where dosing schedules are fairly rigid, this can prove difficult. A small study of patients with PD in a nursing home noted patients were very likely to spend a high proportion of their day in the “off” state and have significant motor impairment. Dietary considerations with levodopa/carbidopa also make it a difficult medication to administer. Preferably, it should be taken on an empty stomach, and dietary protein should be avoided close to medication administration. This is because of the body’s preferred uptake of dietary protein when exposed to levodopa/carbidopa, which can result in a decreased blood level as well as a delay in “on.” However, as the disease progresses and levodopa is taken more often, this is made much more difficult; therefore, an appropriate patient counseling point for people with PD would be to keep protein intake as consistent as possible and to adjust levodopa doses as needed to account for the patient’s protein intake.
The dopamine agonists are still considered by many to be first-line therapy to delay use of levodopa/carbidopa. However, the elderly patient is more likely to experience the hallucinations and confusion that can be seen with the dopamine agonists. In 2009, the Positive Beers criteria, which suggest potentially beneficial medications in certain contexts, noted a preference for the use of ropinirole in the elderly (in addition to stating a preference for levodopa and entacapone), although this recommendation was not supported by evidence. Sleep attacks, the experience of suddenly and unexpectedly falling asleep, are a problem with increasing dopamine by any means but are seen with increased incidence in those receiving dopamine agonists. Case reports of repetitive, compulsive behaviors, such as gambling, eating, drinking, and sexual behaviors, are becoming more common. And although the elderly are not specifically more prone to these behaviors when compared to a younger cohort, this has become an important counseling point for patients and caregivers. Ropinirole immediate release and controlled release and pramipexole immediate release are currently available as nonbranded products. Rotigotine patch offers a novel drug-delivery mechanism for patients with PD in a patch applied once daily to the skin. This can benefit patients with the swallowing difficulties seen in PD. However, those 75 and older account for <10% of enrolled individuals, and it is unknown how the skin changes that occur with aging affect the efficacy of this product. A dopamine agonist withdrawal syndrome has been described in the literature, and while elderly patients are not necessarily at increased risk, it is important to note this potential adverse effect in those whose dopamine agonist is being decreased or discontinued.

The monoamine oxidase type B inhibitor, selegiline, has an amphetamine-like metabolite, which can be a problem in a person with concomitant hypertension or cardiovascular disease. This metabolite may decrease appetite and, therefore, has the potential to cause weight loss. Insomnia is also believed to be a side effect of selegiline, and typically the last dose of the day is given no later than noon. Rasagiline is without an amphetamine-like metabolite and could potentially be a less bothersome agent. A small subgroup analysis showed no age-related effect on experiencing an adverse event with the use of rasagiline. The drug interaction profile of the monoamine oxidase inhibitors is quite extensive, making their use in the elderly difficult, given the extensive polypharmacy seen within the population. Rasagiline trials, however, included participants on a number of drugs and drug classes stated to be contraindicated within the package insert. Fluoxetine and fluvoxamine, however, were not used likely because of their long half-lives. Clinically, PD patients can use concomitant SSRIs typically without incident. However, close monitoring of blood pressure, specifically, and other symptoms of serotonin syndrome is warranted if monoamine oxidase type B inhibitors are used concomitantly.

**KEY POINT:** Concomitant use of rasagiline with SSRIs is common, and selected SSRIs have been used in combination with rasagiline in clinical trials. However, close monitoring of blood pressure and other symptoms of serotonin syndrome is extremely important in the first few weeks of concomitant therapy.

The catechol-O-methyltransferase (COMT) inhibitor, tolcapone, has significant monitoring associated with its use because of reports of hepatotoxicity and is, therefore, rarely used clinically. Entacapone is typically well tolerated overall and is available in a combination tablet with levodopa/carbidopa for ease of dosing. The cost of the combination product is typically similar to buying each agent separately; however, this fixed dose combination does not allow for easy tailoring of levodopa doses. There has been concern raised regarding an increased risk of MI with entacapone, however, there is also evidence of no increased risk.
The anticholinergics, benztropine and trihexyphenidyl, are typically used for treating bothersome tremor. However, these agents are a poor choice in an elderly patient because of their cadre of side effects, including constipation, urinary retention, dry mucous membranes, tachycardia, and, most disturbing in an elderly patient, confusion. Because of their risk-benefit ratio, these agents are included on the Beers criteria. Another agent with anticholinergic activity, in addition to its other effects, is amantadine. It is used most often to treat dyskinesias and has an increased risk of CNS side effects in the elderly patient, such as confusion and psychosis. Of particular note for the elderly patient, amantadine requires dose adjustment for renal impairment.

Apomorphine, an agent available for relief of freezing episodes, is a subcutaneously delivered dopamine agonist. The most distressing side effect of this medication is the extreme hypotension that can be seen shortly after a dose is given. The manufacturer requires the first dose to be given in the care provider’s office or under their care. This hypotension can increase the risk of falls and subsequent fracture. The agent can also cause nausea and vomiting, which typically requires scheduled dosing with an antiemetic such as trimethobenzamide. However, the 5HT3 receptor antagonists (e.g., ondansetron) are absolutely contraindicated due to the risk of additive hypotension.

Disease-Related

Autonomic dysfunction is a common occurrence in PD, manifesting as one or more of the following: constipation, urge urinary incontinence, orthostatic hypotension, sexual dysfunction, seborrhoeic dermatitis, profuse sweating, sialorrhea, and thermal dysregulation. Although no clinical trials exist to address these autonomic abnormalities in the elderly with PD specifically, general treatment principles outlined elsewhere in this text are prudent management. Avoidance of medications that may exacerbate these conditions is especially important, when practical. An interesting clinical dilemma is the patient with orthostatic hypotension and concomitant hypertension. Usually, these individuals are on antihypertensive medications, as their blood pressures can be significantly elevated when in the supine position. If the patient can safely be taken off the antihypertensive, every effort should be made to do so. However, if this is not possible, the addition of fludrocortisone or midodrine may help. The patient should be educated to avoid lying in the supine position when one of these medications is given in order to avoid extremely high blood pressure.

PD may cause drowsiness or lethargy, and many of the medications used to treat the symptoms of PD may cause drowsiness. While the AAN practice parameter supports the use of modafinil in this instance, its use in the elderly, especially those with concomitant cardiovascular disease, is questionable. Sleep patterns are often disrupted in PD. Insomnia may also occur as a result of uncontrolled PD symptoms or restless legs syndrome, a concomitant syndrome with PD. Often, maximizing PD therapy around bedtime can ameliorate this, as well as education on proper sleep hygiene. Chapter 13 provides information on treatment of insomnia that can be applied to patients with PD.

Anosmia or hyposmia can be a presenting symptom of the disease. This inability to smell, and thereby taste, is especially concerning in elders who have stopped eating or decreased eating because they are no longer able to taste, and thereby enjoy, their food. This can lead to weight loss, which in a nursing home resident is monitored closely but is a concern in any senior individual.

Depression, dementia, and psychosis occur in the PD population with increased frequency over age-matched counterparts. Although the disease process can be implicated in these psychiatric nonmotor complications, medications must always be reviewed to ascertain whether these psychiatric manifestations may be an untoward side effect. Depression can be seen in approximately 50% of patients with PD at some point in their disease course, and
although there is no specific literature existing for the elderly with PD, SSRIs are typically employed in clinical practice with good results.\textsuperscript{48} The Movement Disorder Society makes mention that there is evidence to support the antidepressant effect of pramipexole, and that the tricyclic antidepressants (TCAs) nortriptyline and desipramine are “likely efficacious.”\textsuperscript{75} However, multiple trials assessing the efficacy of SSRIs in patients with PD and depression have noted efficacy and present a safer alternative to the TCAs. Dementia in PD is also experienced with increased frequency as the disease progresses. The ChEs rivastigmine and donepezil both have level B evidence to support their use in dementia associated with PD; however, rivastigmine is the only FDA-approved product for this indication.\textsuperscript{76}

Psychosis, typically resulting from medications, is especially burdensome and is a common reason for nursing home placement.\textsuperscript{50} Hence, dopamine agonists are used cautiously in the elderly with PD. When symptoms are controlled on a PD medication regimen and psychosis is experienced, the clinician may elect to treat the psychosis, rather than change the regimen. The atypical antipsychotics quetiapine and clozapine are the first- and second-line agents, respectively, for treating this side effect.\textsuperscript{77,78} And whereas the dopamine antagonism of the antipsychotic medications as a class would seem to contribute to disease exacerbation, these two agents do not. When quetiapine is not effective, or side effects to this agent prevent its use, clozapine is employed. However, the agranulocytosis seen with this agent requires significant monitoring, which can be burdensome to patients, caregivers, and providers.

**KEY POINT:** Quetiapine and clozapine are appropriate choices for the treatment of psychosis that may be experienced secondary to PD therapies, as they decrease psychotic symptoms yet do not exacerbate PD symptoms.

Slowness of movement is not limited to the extremities, and many patients with PD experience slowing of the GI tract, which may manifest as swallowing difficulties, delayed gastric emptying, and constipation. Swallowing difficulties in PD must always be at the forefront of any care plan for the elderly. This includes both the therapies used to treat PD as well as other disease states. Crushing medications to help with administration is common when swallowing problems occur. However, it is prudent to consider a medication regimen review when crushing medications is employed, as long-acting or enteric-coated formulations may need to be changed. Non-oral routes may also be considered when swallowing becomes difficult. With regard to constipation, the product containing polyethylene glycol 3350 has evidence of benefit in PD but must be used on a scheduled basis to have an effect.\textsuperscript{74}

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**Seizures**

**Etiology, Epidemiology, and Clinical Presentation of Seizures**

A seizure is an abnormal electrical activity in the brain manifesting with or without convulsions. Elderly patients may experience a single seizure as a result of electrolyte abnormalities or other acute illness. Epilepsy is a disease manifested by multiple seizures. Status epilepticus is typically defined as continuous seizure activity of 30 minutes or more, or multiple seizures without full recovery of consciousness between seizures.\textsuperscript{79}

Cerebrovascular disease is the most common cause of new-onset seizures in seniors, with poststroke seizures accounting for ~55% of new-onset seizures in this population.\textsuperscript{80} Those who experience a stroke in the cortical region of the brain are more likely to have seizures than those with a stroke in subcortical regions. Brain tumors, trauma, and dementias are other causes of new-onset seizures in this population.\textsuperscript{81,82} Iatrogenic causes must always be ruled
out, with offending agents removed as quickly as possible. Status epilepticus occurs at a higher incidence in the elderly, with almost twice the incidence of the general population, and a much higher mortality rate. Status epilepticus that occurs along with an ischemic stroke has been shown to increase the risk of mortality by three times compared to ischemic stroke alone.

Seizures typically fall into one of two categories, partial or generalized. Partial seizures start in one hemisphere of the brain and manifest as unilateral motor symptoms. If consciousness is not lost, these are deemed simple partial seizures; however, with loss of consciousness, these are categorized as complex partial seizures. Generalized seizures involve both hemispheres of the brain and manifest as bilateral motor involvement. The tonic-clonic seizure is an example of a generalized seizure. If a seizure starts as a partial seizure, but becomes generalized, these seizures are deemed secondary generalized and are typically treated as partial seizures. Generalized absence seizures are typically manifested without motor symptoms but with a sudden “interruption of ongoing activities, a blank stare and possibly a brief upward rotation of the eyes.” In general, absence seizures occur in a much younger population and will not be addressed in this chapter.

The clinical presentation of seizures in the elderly may differ from the presentation in younger people. For instance, seniors are less likely to have auras associated with their seizures. Seizures in a senior population may also be confused with an acute confused state, or syncope, which makes the diagnosis of a seizure in an elderly person quite difficult. Generalized seizures are also less common in the elderly than in a younger group, and partial seizures are much more common. Although clinical presentation may be different, seizures can have a significant impact on quality of life in the elderly, just as they do in younger people with seizures.

**KEY POINT:** The acetylcholinesterase inhibitors and memantine have the potential to decrease seizure threshold and should be used with caution in those with a prior history of seizure disorder.

**Summary of Standard Treatment**

The goal of any treatment for epilepsy is to acutely stop the clinical and electrical seizure activity and to prevent future seizures. A single seizure may not require chronic therapy, especially if an underlying illness is corrected. Although a common primary endpoint of seizure medication trials is a decrease in seizure frequency by 50%, the goal number of seizures in an individual is always zero. Minimizing side effects, maximizing quality of life, and retaining independence and confidence are goals of treatment in all patients.

Standard treatment of seizures depends on the type of seizure being treated. Status epilepticus typically is treated with an intravenous benzodiazepine first-line, followed by either intravenous phenytoin or intravenous fosphenytoin.

Table 12-7 identifies the agents recommended for monotherapy of newly diagnosed epilepsy, for refractory epilepsy, and as add-on therapy by AAN and the American Epilepsy Society. Initial choice of an agent should be individualized, and all agents listed have efficacy data to support their use. However, the International League Against Epilepsy (ILAE) evidence review notes level A evidence for carbamazepine, levetiracetam, phenytoin, and zonisamide as initial monotherapy in partial-onset seizures in adults. Forty to fifty percent of adults who are refractory to the first antiepileptic drug (AED) they are given will have adequate seizure control on another AED as monotherapy. However, if two agents as monotherapy at maximum dosages are ineffective, adjunctive therapy should be considered. Valproate is the supported treat-
ment of first choice for generalized seizures, and, for generalized tonic-clonic seizures refractory to treatment, adjunctive therapy with topiramate is recommended based on safety and efficacy data.93

The SANAD Study Group trials were large, open-label trials designed to best reflect clinical practice in that providers were able to change agents if it was deemed there was treatment failure or intolerability.96,97 There were two arms of the study: one for the treatment of partial epilepsy and another for the treatment of generalized or otherwise unclassified epilepsy.96,97 In the first arm, investigators studied carbamazepine, gabapentin, lamotrigine, oxcarbazepine, and topiramate as monotherapy for the treatment of new-onset partial epilepsy. The majority of the individuals randomized had never received a prior therapy. The median age was 38.3 years old, and the time to treatment failure (defined as stopping of the medication because of either intolerable side effects or inadequate seizure control) was statistically significantly better in the group receiving lamotrigine, with carbamazepine and oxcarbazepine both having statistically significant results as well. In the time to 12-month remission, another primary endpoint, lamotrigine was found to be noninferior to carbamazepine.97 In the second arm of SANAD, individuals with generalized or otherwise unclassified epilepsy were randomized to either valproate, lamotrigine, or topiramate. Valproate showed superiority in both primary endpoints of time to treatment failure (defined as above) and time to 12-month remission.97 However, the median age in the B arm of SANAD was 22.5 years.

In 2008, the FDA completed an analysis of trials in which AEDs were compared to placebo for a variety of conditions (e.g., epilepsy, psychiatric disorders, migraines) and determined an increased risk of suicidal thoughts and behaviors was associated with treatment with an AED. Warnings are now included in the package labeling to this effect, and a Medication Guide is required to be given with each dispensation of an AED, for any indication.

Review of Evidence Supporting Treatment Recommendations in the Elderly

The goals of therapy for a senior patient are no different than those for younger patients, with an additional goal of minimizing drug interactions, because of the increased number of medications seniors typically take. Seniors are typically excluded from trials of AEDs, as is the case with many disease states despite the fact that those over age 60 account for 25% of new cases of epilepsy.98 The exclusion of seniors from trials is due to their high number of comorbid conditions and, thus, medications taken, as well as the increased risk of side effects that could impact safety data presented. Even when they are included in trials of seizure medications, criteria often eliminate those with severe chronic disease (which is typically ill-defined in the literature), psychiatric disease, other neurological illnesses, and even those who are receiving medications known to interact with the agent being researched. A prime example is a study done to assess the tolerability and safety of oxcarbazepine, which utilized the pharmaceutical company’s database.99 Of 1,626 patients in oxcarbazepine trials, 52 (3.2%) were older than 65, and 18 (1.1%) were older than 75. Trials involving the senior population are often small, open-label, prospective, single-center trials, limiting the ability to apply the results to the general senior population. The few agents that have looked at efficacy, safety, and quality-of-life measures specifically in the elderly are lamotrigine, carbamazepine, topiramate, oxcarbazepine, and levetiracetam.

By far, the most widely researched AED in the elderly is lamotrigine. It has shown efficacy as both monotherapy and in combination with other therapies, as well as better tolerability when compared to other therapies, most notably carbamazepine.100-104 Most trials are in elderly patients with any type of seizure, but lamotrigine was studied specifically in those who had an ischemic stroke and developed seizures, and although it was a small study, there was no
Table 12-7. Seizure Medications: Indications and Common Dosages

<table>
<thead>
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<th>Agent</th>
<th>Seizure-Related Indications(^a)</th>
<th>Common Daily Dosages(^b)</th>
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</table>
| Carbamazepine       | Partial seizures with complex symptomatology  
Generalized tonic-clonic  
Mixed seizure patterns  
Monotherapy for newly diagnosed | 800–1,200 mg/day\(^c\)         |
| Ezogabine           | Adjunct for partial-onset seizures                                                               | 300–900 mg/day\(^c\)       |
| Felbamate           | Monotherapy or adjunctive therapy for partial seizures ± secondary generalization\(^d\)          | 2,400–3,000 mg/day\(^c\)   |
| Fosphenytoin        | Control of generalized SE  
Prevention and treatment of seizures during neurosurgery                                             | SE: loading dose 15–20 mg PE/kg with a rate of 100–150 mg PE/min  
Nonemergent: loading dose 10–20 mg PE/kg IV or IM  
Maintenance dose 4–6 mg PE/kg/day IV or IM\(^e\) |
| Gabapentin          | Adjunct for partial seizures ± secondary generalization  
Monotherapy for newly diagnosed  
Add-on for refractory epilepsy                                                     | 900–2,400 mg/day\(^e\)  
Adjust dose for renal insufficiency                                                  |
| Lacosamide          | Adjunctive therapy for partial onset seizures                                                    | 200–400 mg/day\(^c\)  
Adjust dose for renal insufficiency                                                  |
| Lamotrigine         | Adjunctive for primary generalized tonic-clonic  
Adjunctive for partial seizures  
Monotherapy for newly diagnosed  
Mono- or add-on therapy for refractory epilepsy (although evidence for monotherapy in this setting is weaker) | 225–375 mg/day\(^c\)  
Regimens with valproic acid: 100–400 mg/day\(^c\)  
Regimens with an enzyme-inducing AED: 300–500 mg/day\(^c\)  
Adjust dose for renal insufficiency                                                  |
| Levetiracetam       | Adjunctive therapy for partial seizures  
Adjunctive therapy for myoclonic and/or primary generalized tonic-clonic  
Add-on for refractory epilepsy                                                       | 2,000–3,000 mg/day\(^c\)  
Adjust dose for renal insufficiency                                                  |
| Oxcarbazepine       | Monotherapy or adjunctive therapy for partial seizures  
Monotherapy for newly diagnosed  
Mono- or add-on therapy for refractory epilepsy                                           | 1,200–2,400 mg/day\(^c\) |
| Perampanel          | Adjunct for partial seizures                                                                      | 8–12 mg/day               |
| Phenobarbital       | Management of generalized tonic-clonic  
Management of partial seizures  
Monotherapy for newly diagnosed                                                      | 100–300 mg/day\(^c\)   |
<table>
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<tr>
<th>Agent</th>
<th>Seizure-Related Indications&lt;sup&gt;a&lt;/sup&gt;</th>
<th>Common Daily Dosages&lt;sup&gt;c&lt;/sup&gt;</th>
</tr>
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| Phenytoin   | Management of generalized tonic-clonic seizures  
Seizure prevention in head trauma/neurosurgery  
Monotherapy for newly diagnosed                      | 300–1,200 mg/day<sup>c</sup>                                           |
| Pregabalin  | Adjunctive therapy for partial seizures                                                              | 150–600 mg/day<sup>c</sup>  
Adjust dose for renal insufficiency                   |
| Primidone   | Management of grand mal, psychomotor, or focal seizures                                               | 750–1,500 mg/day<sup>c</sup>                                           |
| Rufinamide  | No adult indications at present.                                                                     | 1,600–3,200 mg/day<sup>c</sup>                                         |
| Topiramate  | Monotherapy or adjunctive therapy for partial seizures  
Monotherapy or adjunctive therapy for tonic-clonic  
Monotherapy for newly diagnosed  
Mono- or add-on therapy for refractory epilepsy       | Monotherapy: 100–400 mg/day<sup>c</sup>  
Adjunctive partial: 100–200 mg bid  
Adjunctive tonic-clonic: 200 mg bid                    |
| Tiagabine   | Adjunctive therapy for partial seizures  
Add-on for refractory epilepsy                        | Regimens with enzyme-inducing AEDs: 32–56 mg/day<sup>c</sup>             |
| Valproic acid | Monotherapy or adjunctive therapy for complex partial seizures  
Monotherapy or adjunctive therapy for simple or complex absence seizures  
Monotherapy for newly diagnosed                      | 15–60 mg/kg/day<sup>c</sup>                                             |
| Vigabatrin  | Refractory, complex partial seizures                                                               | 1,000–3,000 mg/day<sup>c</sup>                                         |
| Zonisamide  | Adjunctive therapy for partial seizures  
Add-on for refractory epilepsy                        | 100–400 mg/day<sup>c</sup>                                             |

IM, intramuscular; IV, intravenous; PE, phenytoin equivalents; SE, status epilepticus.

<sup>a</sup>Indications applicable to older adults.

<sup>b</sup>Indicates common total daily dosages.

<sup>c</sup>In divided doses.

<sup>d</sup>Not indicated for first-line therapy.

See reference 128 for additional information.
difference in seizure frequency with lamotrigine versus carbamazepine. However, there was increased tolerability with lamotrigine. Carbamazepine in these trials, although less tolerable than lamotrigine in this population, was noted to be efficacious for seizures in the elderly. A small, open-label study of patients aged 60 and older who wished to change AED, either because of intolerable side effects or continuing seizures, were given a trial of lamotrigine first as add-on therapy and then as monotherapy, if they wished. In those patients who chose to convert to lamotrigine monotherapy, 64% achieved seizure freedom. And, in an analysis of over 400 patients over the age of 55, lamotrigine was the most effective at decreasing seizure frequency and showed the best tolerability profile when compared to 10 other antiepileptic medications.

Topiramate has some data to support its use as monotherapy in the elderly in a small trial and a subgroup analysis of a larger seizure trial. Both showed similar efficacy to trials in younger patients, with seizure freedom ranging from 63% at 7 months and 44% at 12 months. Adverse effects were dizziness, nausea, loss of appetite, and paresthesias. Of note, there was a statistically and clinically significant decrease in weight from baseline in one of the trials.

A small subgroup of elderly patients within a larger clinical trial of oxcarbazepine as monotherapy for partial seizures showed good response in the 12-month remission rates among the seniors in the cohort (n = 19). There was no breakdown within the subgroup in regard to adverse events. However, a retrospective analysis of the elderly patients within a large database of trials of oxcarbazepine as monotherapy showed similar safety and tolerability with oxcarbazepine compared to the remainder of the cohort, although the number of seniors was small. Hyponatremia, vertigo, nausea, and abnormal vision were more common in the elderly than in the younger drop-outs. This analysis did not assess efficacy.

A small study of levetiracetam monotherapy in poststroke patients with at least two seizures showed seizure freedom at 4 months in 85%. One person discontinued treatment due to intolerable somnolence. A retrospective chart review of elderly patients with partial epilepsy receiving levetiracetam noted good response and relatively good tolerability, and in a retrospective chart-review of over 400 patients, levetiracetam showed good efficacy in decreasing seizures, as well as good tolerability in the elderly with new onset seizures. In an observational study of Alzheimer patients with new-onset seizures, a trial of levetiracetam was given after removal of all medications that could increase risk of seizures, including their CI and any neuroleptic they were receiving. At a dose of 1,000–1,500 mg/day, levetiracetam was associated with seizure freedom in 18 of the 25 patients; 4 patients discontinued the drug because of intolerable side effects, including somnolence, gait disturbance, agitation, and increased confusion. However, it is unclear whether discontinuation of other therapies could have confounded these adverse events.

Many trials of AEDs look specifically at tolerability in the elderly population, relying on efficacy data from the younger cohort. However, given the differing etiologies of seizures in the senior population, this extrapolation of data should be done with caution. Elderly patients also tend to achieve seizure control with lower doses of AEDs and at lower AED serum levels than younger people. This begs the question of whether serum monitoring should be done in an elderly patient if lower AED serum levels are effective. A position paper by the ILAE Commission on Therapeutic Strategies suggests therapeutic drug monitoring in the elderly after a newly-started AED has reached steady state to determine the individual’s therapeutic concentration. They also recommend therapeutic drug monitoring when doses of interacting medications are being adjusted. The ILAE also support measuring the unbound concentrations of AEDs known to be highly protein-bound.
KEY POINT: Because of the potential for low albumin in the elderly, it is appropriate to measure unbound concentrations of highly protein-bound AEDs.

The treatment of status epilepticus in the elderly typically follows that of the general population. No specific evidence supporting or refuting current guidelines in the elderly subpopulation exists.

There is currently no evidence to suggest an increase in suicidal behaviors or thoughts specifically in the elderly, and given the low numbers of elderly in trials of these agents, conclusions are not likely to be drawn. However, the FDA’s new warnings and the receipt of a Medication Guide with each AED prescription include those dispensed to seniors.

**Common Problems Encountered in the Senior Population with Seizure Disorder**

A common clinical problem in the care of the older adult is encountering the prescription of an AED prescribed in the poststroke period. Questions can arise regarding the necessity of a long-term AED, as well as whether it is appropriate or not if the patient only had one seizure after the stroke. The incidence of poststroke epilepsy is 5% to 15%, and most major societies advise against primary prophylaxis for seizures in the poststroke period. However, when a senior has a seizure, the risk of a second seizure depends on when the seizure occurred. For those seniors with an early-onset seizure (within 7 days of the stroke, but typically within 24 hours), the incidence of another seizure is less than 43%. However, in those with late-onset seizures (more than 7 days after the stroke), the potential for a second seizure can range from 50% to 60%. Because of this increased risk, many clinicians will choose to provide long-term secondary prophylaxis. It is important to note that there is scant data to support this practice, and typically if a senior is put on this type of prophylaxis, he or she will likely be on it for the long term. The patient would then need to be seizure-free for 2-5 years and have a normal EEG to be considered for withdrawal of the AED. The choice of whether to provide prophylaxis or not should be done in concert with the patient or his or her caregiver, weighing the risks of an AED alongside the risk of another seizure.

Seniors, high consumers of healthcare, can be more prone to the drug interactions and untoward side effects of AEDs. The pharmacokinetic and pharmacodynamic changes associated with aging also make the choice of AED somewhat difficult. Whereas many newer-generation AEDs tend to be better tolerated, the cost associated with the agents themselves can be a limiting factor to their use in the senior population.

**Agent-Related**

Despite being used frequently in the elderly with seizure disorder, phenytoin has many issues associated with its use, especially long term. It induces many CYP450 isoenzymes, making it highly likely to interact with many common medications used in the elderly, and decrease blood levels of common vitamins, such as B6, B12, and vitamin D. When given concomitantly with tube feedings, its bioavailability is significantly reduced, putting patients at risk for lower blood levels and also increased risk for seizures. Tube feedings should be stopped for 2 hours prior to phenytoin administration and should be held for at least 1 hour after phenytoin administration. This can be very difficult in someone receiving twice-daily administration of phenytoin on continuous tube feeds, and in most cases if this cannot be done easily, switching to another AED is often employed. However, in those whom phenytoin is unable to be stopped, doses may be increased to compensate for this interaction. However, it is of the utmost importance to be consistent with dosing and to remember dosage adjustments have been made should the tube feeding be stopped for any length of time or discontinued. Phenytoin can increase the risk for falls by both inducing vitamin D metabolism, as well as the
potential to cause cerebellar atrophy with long-term use. In order to assess true steady state, levels should be drawn 2–3 weeks after starting phenytoin in the elderly because of increased half-life in this population. And because it is highly protein bound, a free phenytoin level should be drawn in a frail elderly patient who is likely to have hypoalbuminemia, rather than a total phenytoin assay.

Phenytoin can block alpha-receptors and, thereby, may decrease internal bladder sphincter tone, which can exacerbate stress urinary incontinence. The gingival hyperplasia seen in a younger cohort is not typically seen in the elderly. Fosphenytoin has very little research specifically in the elderly; however, its ability to induce many P450 isoenzymes makes its use in the elderly difficult. But it is typically only used short term in emergent situations, or when the oral route of administration is not available in a patient receiving phenytoin.

**KEY POINT:** If phenytoin doses are increased to compensate for decreased absorption because of tube feedings, it is of utmost importance to be consistent with dosing and to remember doses have been adjusted if tube feedings are stopped for any length of time or discontinued.

Hyponatremia, rash, and syndrome of inappropriate secretion of antidiuretic hormone are side effects that can occur with carbamazepine; however, they can be seen with increased frequency in the elderly. Because of its induction of many CYP450 isoenzymes, carbamazepine is highly likely to interact with many medications commonly found on the profiles of elderly patients. Carbamazepine also induces its own metabolism. It binds to alphaglycoprotein (known to increase in the elderly), which can make total carbamazepine levels look falsely therapeutic. Carbamazepine can induce vitamin D metabolism, potentially leading to an increased risk of osteoporosis and falls. Overflow incontinence, secondary to increased parasympathetic stimulation of the detrusor, is also an untoward consequence of carbamazepine use commonly overlooked. Similar to carbamazepine, oxcarbazepine has an increased risk of hyponatremia in the elderly and can decrease the efficacy of estrogen, something to note in an individual receiving estrogen-replacement therapy. Oxcarbazepine also has evidence to suggest an increased risk of MI and stroke compared to carbamazepine.

Valproic acid is commonly used in elderly patients. Its time to steady state may be doubled in an elderly cohort, so this should be taken into consideration for drug monitoring. Platelet count and ammonia levels should be monitored and, in those with hypoalbuminemia, the unbound concentration should be tested. Weight gain and a fine hand tremor may also be seen in the elderly receiving valproic acid.

Phenobarbital, another older agent, should be used in the elderly with extreme caution, if at all, because of its long half-life and ability to cause cognitive disturbances. It can also interfere with vitamin D metabolism and is highly protein bound, which can be an issue in an elderly patient with decreased albumin. Like oxcarbazepine, there is some evidence to support an increased risk of MI and stroke with phenobarbital when compared to carbamazepine. Due to additive respiratory depression, phenobarbital is contraindicated with the concomitant use of an opioid. It is noted as a drug to be avoided in the elderly and is associated with dependence. Primidone, the parent drug of phenobarbital, has the same issues and warnings. When discontinuing these agents, doses should be tapered slowly to avoid withdrawal reactions.

Gabapentin’s ability to cause weight gain is well documented in the literature in the young and is also seen in the elderly in clinical practice. Elderly are much more prone to the effects of ataxia and somnolence, however. Gabapentin has the potential to cause edema, yet is commonly overlooked when iatrogenic causes are being investigated. Pregabalin has a similar side effect profile.
Lamotrigine is well known for the potential to cause a rash, which can occur at any time during its use, but most often is seen in the titration phase. A Stevens-Johnson syndrome–type rash may also occur in patients taking lamotrigine; therefore, any complaint of rash needs to be quickly addressed, given the life-threatening nature of this particular syndrome. This risk for rash is increased in those receiving concomitant valproic acid. However, with slow titration, over more than 8 weeks, this adverse effect can be minimized. This need for slow titration limits its use to those who do not need immediate therapeutic doses of their seizure medication.

Levetiracetam’s literature support in the elderly has been growing in recent years. This is owed in large part to very few drug interactions, no protein-binding, and a perception of a mild side effect profile, compared to other AEDs. This has largely been supported in clinical trials. However, levetiracetam must be dose-decreased in renal dysfunction and, like the other AEDs, has growing evidence of the potential to contribute to low bone mineral density. Topiramate’s most common side effect in the elderly is weight loss. On average, in small clinical trials in the elderly, patients lost ~5 pounds, with a subgroup analysis noting those with an increased body mass index (BMI) losing the most weight.\(^\text{106, 107}\) Cognitive disturbance and word-finding difficulties can be experienced in the elderly on topiramate. In younger patients, topiramate has an increased risk of kidney stones, which should be monitored in the elderly, especially those with decreased water intake or on water restriction due to other disease states, such as congestive heart failure.

Zonisamide is rarely used in the elderly, for several reasons. It should be used with caution in those with a creatinine clearance <50 mL/min and in those allergic to sulfonamides. Zonisamide may also increase the risk of renal stones, so like topiramate it should be used with caution in those with low water intake. Zonisamide has also been implicated in causing cognitive impairment and psychosis as well as increasing the chance of metabolic acidosis.

Several AEDs have not been evaluated in older adults. Ezogabine has not been evaluated in the elderly, but because of issues with eye abnormalities, sometimes leading to vision loss and blue-skin pigment changes, this will likely remain a last-line adjunctive agent. Ezogabine can also cause urinary retention, hallucinations, and QT prolongation, which can be problematic in an elder. Lacosamide should be used with caution in those with conduction disorders as it has the potential to prolong the PR interval. It should be avoided in those with congestive heart failure and in those who are taking other medications that prolong this interval. Perampanel can cause significant neuropsychiatric issues, including agitation and aggression, as well as gait disturbances and dizziness. Rufinamide is indicated only as adjuvant therapy for generalized seizures secondary to Lennox-Gastaut, a type of epilepsy seen in children. It can shorten the QT interval and must be used with caution in those patients with pre-existing conduction disorders and in those on concomitant QT interval shortening medications. Tiagabine can result in Stevens-Johnson syndrome or toxic epidermal necrosis, albeit rarely, as well as cognitive slowing. It is also highly protein bound, so free concentration should be measured if therapeutic drug monitoring is undertaken. Vigabatrin’s boxed warning regarding permanent vision loss in up to a third of people who take the drug is the rationale behind its use only in refractory cases of complex partial seizure disorder. It can also cause issues with psychosis, peripheral edema, and anemia.

As with any pharmacotherapeutic intervention, the medication cannot work if the patient does not take it, and adherence to the AEDs can be difficult in the elderly. Two risk factors have been elucidated in the literature that increase the likelihood of nonadherence to AEDs by the elderly: impairment of cognitive function and weight gain.\(^\text{122}\) The incidence of these side effects should definitely be taken into account when starting a new AED in an elderly patient as well as when nonadherence is suspected.
Disease-Related

Many medications and herbal products commonly used by the geriatric population may lower seizure threshold (see Table 12-8). It is important to avoid the use of these medications whenever possible in a patient with seizure disorder. If a patient should have a new onset seizure, a thorough medication review should take place, ensuring the patient is asked about over-the-counter product use as well as herbals.

Certain AEDs are excreted by the kidneys. Dose adjustments are frequently required in elderly patients because of renal insufficiency. Table 12-7 notes the agents that necessitate this modification.

Table 12-8. Medications and Dietary Supplements That Decrease Seizure Threshold

<table>
<thead>
<tr>
<th>Medication</th>
<th>Dietary Supplement</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bupropion</td>
<td>Lithium</td>
</tr>
<tr>
<td>Cephalosporins</td>
<td>Ma huang</td>
</tr>
<tr>
<td>Cholinesterase inhibitors</td>
<td>Maprotiline</td>
</tr>
<tr>
<td>Duloxetine</td>
<td>Meperidine</td>
</tr>
<tr>
<td>Ephedrine</td>
<td>Memantine</td>
</tr>
<tr>
<td>Fluoroquinolones</td>
<td>Metoclopramide</td>
</tr>
<tr>
<td>Fluvoxamine</td>
<td>Penicillins</td>
</tr>
<tr>
<td>Ginkgo biloba</td>
<td>Phenothiazines</td>
</tr>
<tr>
<td>Ginseng</td>
<td>St. John’s wort</td>
</tr>
<tr>
<td>Insulin</td>
<td>Theophylline</td>
</tr>
<tr>
<td>Isoniazid</td>
<td>Tramadol</td>
</tr>
<tr>
<td>Kava kava</td>
<td>Tricyclic antidepressants</td>
</tr>
<tr>
<td></td>
<td>Venlafaxine</td>
</tr>
</tbody>
</table>

See reference 91 for additional information.

Several enzyme-inducing AEDs have been implicated in the literature as increasing the risk of osteoporosis. However, there is emerging evidence that this might be a class effect. Regardless of the cause of decreased bone mineral density (BMD) or osteoporosis, this decreased bone strength should be treated. Although there is no FDA-approved agent for the treatment of AED-induced osteoporosis, a small trial of male veterans receiving AED therapy (average age, 60.5 years) noted a statistically significant increase in BMD at the lumbar spine with the use of risedronate 35 mg orally once weekly when added to a regimen of calcium and vitamin D, compared to those receiving just calcium and vitamin D alone. However, it should be noted that there were also BMD gains in those on calcium and vitamin D alone, only more so in the group receiving additional risedronate. For patients using an AED known to induce vitamin D metabolism, it is a prudent recommendation to follow 25-OH vitamin D levels regularly and supplement if necessary. Patients with seizures should be screened on a regular basis for depression and anxiety, as these conditions can be seen with increased incidence in those with seizure disorder. Again, the choice of agent should be chosen with patient- and agent-related variables in mind. Table 12-9 provides other drug-disease interactions to consider when choosing an AED.
### Table 12-9. Antiepileptic Drug-Disease Interactions

<table>
<thead>
<tr>
<th>Selected Conditions</th>
<th>Precaution</th>
<th>Contraindication</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anorexia, weight loss</td>
<td>Felbamate, topiramate, carbamazepine (anorexia), rufinamide, zonisamide (anorexia)</td>
<td></td>
</tr>
<tr>
<td>Cardiac conduction abnormalities, ventricular arrhythmia</td>
<td>Carbamazepine, ezogabine, fosphenytoin, lacosamide, lamotrigine, phenytoin (parenteral), oxcarbazepine</td>
<td>Phenytoin if sinus bradycardia, sinoatrial block, 2nd-or 3rd-degree AV block, Adams-Stokes block, Rufinamide if familial short QT syndrome</td>
</tr>
<tr>
<td>Cognitive impairment</td>
<td>Barbiturates, benzodiazepines, topiramate, tiagabine, zonisamide</td>
<td></td>
</tr>
<tr>
<td>Gait unsteadiness, dizziness</td>
<td>Barbiturates, carbamazepine, felbamate, gabapentin, lacosamide, lamotrigine, levetiracetam, oxcarbazepine, perampanel, phenytoin, pregabalin, rufinamide, tiagabine, topiramate, valproate</td>
<td></td>
</tr>
<tr>
<td>Hepatic disease, impairment</td>
<td>Carbamazepine, ezogabine, felbamate, lacosamide, rufinamide, tiagabine, valproate, zonisamide, oxcarbazepine, perampanel, phenytoin</td>
<td>Felbamate, phenobarbital, valproate</td>
</tr>
<tr>
<td>Hyponatremia</td>
<td>Carbamazepine, oxcarbazepine</td>
<td>Gabapentin</td>
</tr>
<tr>
<td>Narrow-angle glaucoma</td>
<td>Topiramate</td>
<td></td>
</tr>
<tr>
<td>Osteomalacia, osteoporosis</td>
<td>Carbamazepine, levetiracetam, oxcarbazepine, phenobarbital, phenytoin, primidone, valproate</td>
<td></td>
</tr>
<tr>
<td>Respiratory disease (obstructive, dyspnea)</td>
<td>Benzodiazepines, phenytoin (IV, IM)</td>
<td>Phenobarbital</td>
</tr>
<tr>
<td>Tremor (familial, Parkinson disease)</td>
<td>Gabapentin, lacosamide, lamotrigine, pregabalin, rufinamide, tiagabine, topiramate, valproate</td>
<td></td>
</tr>
<tr>
<td>Renal impairment</td>
<td>Ezogabine, gabapentin, lacosamide, levetiracetam, perampanel, phenobarbital, pregabalin, topiramate, vigabatrin, zonisamide</td>
<td></td>
</tr>
<tr>
<td>Sedation</td>
<td>Barbiturates, benzodiazepines, carbamazepine, felbamate, gabapentin, lacosamide, lamotrigine, pregabalin, oxcarbazepine, rufinamide, tiagabine, topiramate, valproate</td>
<td></td>
</tr>
</tbody>
</table>
Table 12-9. Antiepileptic Drug-Disease Interactions (continued)

<table>
<thead>
<tr>
<th>Selected Conditions</th>
<th>Precaution</th>
<th>Contraindication</th>
</tr>
</thead>
<tbody>
<tr>
<td>Urinary incontinence</td>
<td>Carbamazepine, clonazepam, ezogabine, gabapentin, lamotrigine, oxcarbazepine, phenobarbital, phenytoin, tiagabine, topiramate, valproate</td>
<td></td>
</tr>
<tr>
<td>Nephrolithiasis</td>
<td>Topiramate, zonisamide</td>
<td></td>
</tr>
</tbody>
</table>

AV block, atrioventricular nodal block; IM, intramuscular; IV, intravenous.

aHypersensitivity to the antiepileptic drug, its ingredients, or related class of drugs is a contraindication.

bPhenobarbital is commonly believed to impair cognition; however, at equivalent serum drug concentrations, this effect was no different than antiepileptic drugs with an uncertain effect (phenytoin, carbamazepine, oxcarbazepine, valproate).

cCarbamazepine and valproate may pose a lower risk of gait disturbance than other antiepileptic drugs.

dThe risk of osteoporosis with several of the newer antiepileptic drugs is not established.

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Case 1: Delirium

Setting:
Hospital.

Subjective:
GM is a 74-year-old man who presents with a chief complaint of confusion and incontinence. His wife says he became confused about 2 days ago. The confusion at first was minor but worsened until he tried getting into the car and going to work at 5:00 a.m., although he has been retired for 9 years. Today he was incontinent and she brought him to the hospital, where he was admitted for evaluation.

Past Medical History:
MCI for 2 years, hypertension, benign prostatic hypertrophy. Medications prior to admission: lisinopril 10 mg daily, doxazosin 4 mg at bedtime, aspirin 81 mg daily.

Social History:
Retired schoolteacher, lives at home with his wife.

Physical Examination:
Well developed, well-nourished older gentleman. Oriented ×2. Otherwise unremarkable except for pain with palpation at the costo-vertebral angles.

Labs:
BUN 48 mg/dL, serum creatinine 1.8 mg/dL, CBC: WBC 13,000. Urinalysis: positive leukocyte esterase, positive nitrites; CK-MB WNL; troponins WNL. ECG: no change from previous.

Assessment:
Urinary tract infection and delirium secondary to infection.

Plan:
1. Start oral levofloxacin dosed per creatinine clearance.
2. Avoid intravenous lines, urinary catheter, and other tethers.
3. Nonpharmacologic measures for reduction of delirium, including music, massage, redirection, and stimulation during the day; quiet at night.

Rationale:
1. Infections and MIs frequently do not present with the same symptoms in elderly patients as they do in younger adults. Individuals with cognitive impairment from any source may become delirious as a result of the insult. When a patient presents in delirium, work-up must include evaluation for the common precipitants. As this patient did not have any medication changes, a focus on infection or cardiac conditions is appropriate.
2. Levofloxacin is an appropriate antibiotic to choose in a complicated urinary tract infection; however, it has been associated with causing delirium. Appropriate dosing in renal insufficiency will help minimize this effect.
3. Avoiding intravenous lines and urinary catheters when not needed will eliminate the risk of the delirious patient pulling them out, causing more damage. Nonpharmacologic measures such as music therapy, massage, aromatherapy, and behavior techniques have been shown to reduce the risk for delirium and may aid in recovery after delirium has developed. Families or friends may be able to help with these, although some hospitals have specialized units that include volunteers who can implement such measures. Using these nonpharmacologic measures early in the hospitalization will help prevent the need for pharmacologic treatment of delirium and hopefully speed recovery.
Case 2: Parkinson Disease

Setting:
Assisted living facility.

Subjective:
PG is an 86-year-old female patient with a past medical history positive for PD for 3 years. Her PD symptoms have been controlled on levodopa/carbidopa 200/25 mg three times daily for the past 2 years. However, she is currently experiencing “wearing off” before her next dose of levodopa/carbidopa is due, as well as problems “getting moving” when she wakes up in the morning, around 7:00 a.m.

Past Medical History:
PD ×3 years, osteoporosis ×17 years, s/p hip fracture 12 years ago, episodic hypotension, and glaucoma. Her concurrent medications include calcium/vitamin D3 500 mg/200 international units three times daily, alendronate 70 mg once weekly, dorzolamide/timolol 1 drop both eyes twice daily, travoprost 1 drop both eyes at bedtime, aspirin 81 mg once daily, and acetaminophen 650 mg as needed for headache.

Objective:
Ht 5’0˝, Wt 96 lb; BP 131/89 (sitting), 113/79 (standing); P 79 BPM (sitting), 90 BPM (standing); T 98.2°F, RR 17.

Physical Examination:
Resting tremor present R>L, shuffling gait, slight stooped posture.

Assessment:
86-year-old PD patient experiencing wearing off and morning bradykinesia.

Plan:
1. Change dosing interval of levodopa/carbidopa 200/25 mg to four times daily 7:00 a.m., 1:00 p.m., 7:00 p.m., and 11:00 p.m.
2. Counsel patient to take levodopa/carbidopa in the morning before rising from bed and to wait 30 minutes or more for it to take effect.
3. Review medication regimen for issues with administration.
4. Return to clinic in 4 weeks to assess improvement in wearing off and possible dyskinesias.

Rationale:
1. The wearing off PG is experiencing can be attributed to disease progression, and although there are options other than decreasing the dosing interval, PG appears to be tolerating the levodopa/carbidopa well. If possible, it is best to stay with the single drug, levodopa/carbidopa, to avoid additional exposure and risk for adverse effects. Other options are available should this one not be optimal. A dopamine agonist could be added; however, PG is of advanced age and may be more prone to the psychiatric adverse effects of this type of medication. A COMT inhibitor could also be added with each dose of levodopa/carbidopa; however, these are expensive agents and would add to pill burden (unless the combination product, also expensive, was used). Another option is addition of selegiline or rasagiline. Selegiline is the least expensive option, except for the orally-disintegrating tablet, although it offers an important dosing option for the early morning. Rasagiline has been shown effective in this situation and is dosed conveniently at once a day but is more expensive.
2. Due to the swallowing difficulties and slowed GI transit seen with PD, the alendronate has the potential to cause ulceration if it gets caught in the esophagus. And the question must be asked, can she administer her eye drops correctly with possible tremor and rigidity? All medications require reassessment due to the motor and nonmotor deficits seen with PD.

**Case Summary:**
Wearing off between levodopa doses and dyskinesias are common occurrences as PD progresses. Knowing how to manage these occurrences are important concepts. Although there are little data to support specific interventions in the elderly when these occur, keeping the tenets of geriatrics at the heart of the plan is key to success. These include making one intervention at a time in order to best assess efficacy and tolerability, as well as starting low with doses and going slow in titration. Timely reassessment of interventions and continued follow-up are similarly important. Interventions may result in symptom improvement but with concomitant bothersome dyskinesias. And, as the disease process progresses and symptoms worsen, additional intervention may be required.
Chapter Summary

One of the most dreaded diseases associated with aging is dementia, as no preventive treatment has been identified, therapies do not alter its course substantially, and, over time, the patient must rely on around-the-clock care without a clear sense of self. Dementia may have vascular causes, but the most common etiology is AD. CIs are the mainstays of therapy, particularly for mild-to-moderate AD, with memantine an option for those who are intolerant or progress to severe disease. NP symptoms also remain a challenge for treatment as medications have little evidence that efficacy outweighs the risk for side effects in this population.

Delirium, most common in patients with neurologic compromise, is a syndrome of the elderly that complicates therapy of other disease states and can lead to significant morbidity and mortality. Preventive measures have been successful in hospitalized patients. Once a diagnosis of delirium is established, nonpharmacologic measures should be instituted, with pharmacologic therapy reserved for patients who pose safety problems for themselves or others.

As another progressive neurologic disease without cure, PD requires timely re-evaluation of interventions. Levodopa/carbidopa remains the gold standard of symptomatic treatment, and rasagiline has some literature supporting its tolerability in those older than 70. Dopamine agonists are likely not the best first choice in an elderly patient, and, if used, should be titrated slowly and monitored closely for adverse effects. In patients experiencing wearing off or dyskinesias, one must keep the tenets of geriatrics at the center of the plan, avoiding anticholinergics as much as possible due to their myriad side effects.

Seizures, the final neurologic condition covered in this chapter, are common in the elderly, especially among those with a history of stroke, tumors, trauma, and dementia. There is a lack of good-quality trials of AEDs specifically in the elderly population, which makes the choice of an AED even more confusing. Lamotrigine, carbamazepine, topiramate, oxcarbazepine, and levetiracetam have been studied specifically in the elderly population for safety, efficacy, and tolerability, with lamotrigine having the most data in this population. However, given...
the quality of these trials, additional research is urgently needed to help clinicians make an evidence-based decision.

Self-Assessment Questions

1. Why are serum vitamin B12 concentrations measured in the work-up of dementia?
2. What are the important counseling points for a patient who is started on a CI?
3. When would antipsychotics be appropriate in treating a patient with dementia?
4. What are the risk factors for developing delirium?
5. What nonpharmacologic treatments for delirium are useful?
6. What are the pros and cons of starting levodopa/carbidopa versus a dopamine agonist in an elderly patient newly diagnosed with PD?
7. What are the options available to treat the patient who is experiencing wearing off?
8. How do dyskinesias contrast with wearing off?
9. How do the nonmotor complications of PD impact the quality of life in a community-dwelling senior?
10. Which AEDs should have the free concentration measured when conducting therapeutic drug monitoring? Why?
11. Which AEDs should be renally dose-adjusted in an elderly person?
12. What precautions should be undertaken when adding lamotrigine to a valproate-based regimen?
13. What are the advantages and disadvantages of using the newer AEDs for the treatment of partial seizures in the elderly?
14. Why might the diagnosis of a seizure disorder in an elderly person be difficult?

References

the emerging role of systemic low-grade inflammation and adiposity. *Brain Res Bull.* 2010;144–149.


Learning Objectives

1. Recognize the Diagnostic and Statistical Manual of Mental Disorders, 5th edition (DSM-5) criteria for major depressive disorder, anxiety disorders, and features commonly observed in late-life depression and anxiety.

2. Recommend an appropriate treatment plan for a geriatric patient suffering from depression and/or anxiety.

3. Recognize the changes in sleep that occur with normal aging and the impact of insomnia on an elderly patient’s health and quality of life.

4. Recommend appropriate therapy for insomnia based on published evidence in the elderly patient.

5. Describe the limitations of the DSM-5 criteria when used to diagnose elderly patients with substance-use disorders.

6. List the alcohol drinking limits for geriatric patients and discuss the reasons why guidelines suggest lower limits compared to younger adults.

7. Recommend an appropriate treatment plan for alcohol withdrawal and long-term abstinence for a geriatric patient.

Key Terms and Definitions

CLINICAL GLOBAL IMPRESSION OF IMPROVEMENT (CGI-I): Seven-point scale that measures how much a patient’s symptoms have improved or worsened compared to baseline.

COGNITIVE BEHAVIORAL THERAPY: Therapy to help patients correct negative thoughts associated with depression and to cope with anxiety disorders. The therapy includes breathing retraining, muscle relaxation, cognitive restructuring to focus on the consistent worrying, and graded exposure so the patient can learn how to cope in stressful/phobic situations.
Introduction

Psychiatric disorders discussed in this chapter include depression, anxiety, insomnia, and substance abuse. Although diagnostic criteria are the same as for younger adults for these disorders, it is sometimes difficult to elicit clear symptoms of depression or anxiety from older patients, especially if they have underlying dementia. Fortunately, newer pharmacologic agents add options that are better tolerated in individuals with comorbidities, multiple medications, and altered pharmacodynamics.

Sleep architecture and sleep physiology change with aging; comorbidities and the environment contribute to insomnia in the elderly patient. If underlying factors cannot be corrected, comorbidities are not treated and controlled, and nonpharmacologic therapy is ineffective, medications may help the patient achieve sleep goals. However, it is important to choose drug therapy that will minimize adverse events and for the patient to understand how these agents work to set proper expectations.

Finally, substance and alcohol use should not be dismissed as a possible health issue.
in older adults. Alcohol withdrawal can be life-threatening in any age group and is even more of a risk for individuals with heart or lung disease. Psychosocial interventions appropriate to older age groups may be coupled with pharmacologic treatment to maintain sobriety.

**Depression**

*Etiology, Epidemiology, and Clinical Presentation Specific to Geriatrics*

Depression is the most common psychiatric disorder diagnosed in the elderly, with approximately 5% to 15% of community-based elderly individuals meeting criteria for major depressive disorder rising to 14% to 50% in the nursing home population. Often, a depressive episode witnessed in older adults is a recurrence of the disorder that was diagnosed as a young adult. However, 30% of cases are noted to be purely late-onset depression.

Common late-life diseases such as cerebral vascular disease, cardiovascular disease, and dementia often coexist or precipitate late-onset depression. For patients who have suffered a stroke, major depression is noted to develop in 15% to 25% of individuals. Approximately 25% of patients who experience a myocardial infarction or undergo cardiac catheterization develop major depression. The prevalence of depression in patients with Alzheimer dementia is approximately 10% to 20% and noted to be higher in those with subcortical dementias.

**Consequences of Late-Life Depression**

If depression is left untreated, symptoms may persist for years and result in decreased daily function, poor quality of life, and increased rates of suicide and nonsuicidal mortality. Of the more recent large epidemiologic studies found that depressed elderly patients had a significantly increased relative risk of 1.67 for impairment of activities of daily living and 1.73 for mobility impairment compared to nondepressed elderly. Over the last two decades, there have been several studies showing a correlation with depression and increased cardiovascular mortality.

Research has repeatedly shown that depression is associated with cognitive impairment, but the relationship between the two is not clear. Recent large studies have shown depression to be a risk factor for development of mild cognitive impairment (relative risk of 2.35) and dementia (hazard ratio of 2.0), with the risk of vascular dementia being higher than the risk of Alzheimer disease. Studies have also shown the risk of dementia increases with longer duration and higher severity of depressive symptoms. Even after multiple studies, it is still not exactly clear whether depression is a definitive risk factor for dementia later in life or if depression may be a prodromal symptom of dementia.

**Diagnostic Criteria**

Although many clinicians screen for depression using the Geriatric Depression Scale or the other tools discussed in Chapter 4, diagnosis is made using criteria from the DSM-5. A patient meets the criteria for major depressive disorder if he or she experiences either depressed mood or decreased interest or pleasure in usual activities and meets at least four of the following criteria: significant appetite and weight changes, increased agitation or motor retardation, loss of energy, changes in sleep (insomnia or hypersomnia), feelings of guilt or worthlessness, problems with memory or concentration, or thoughts of suicide. According to the DSM-5, symptoms must exist almost daily for at least 2 weeks, lead to functional impairment, and not be the result of substance abuse or other medical conditions.

Other mood disorders, such as persistent depressive disorder (dysthymia) or minor depression, are frequently assessed in the geriatric population, and about 25% of these cases will develop into major depression within 2 years. Minor depressive disorder is not an official DSM-5 disorder but has been defined in the literature as having at least two but fewer than five of the symptoms listed under major depres-
sive disorder for 2 weeks or longer. Persistent depressive disorder is defined as a sad mood on most days with two other symptoms listed under major depressive disorder lasting for 2 years or more. To meet the criteria for depressive disorders, patients cannot have a history of mania or psychotic disorders.

Assessment and Presentation

Noted risk factors for late-life depression include unmarried status, lack of social support, lower socioeconomic status, family history of mood disorders, substance abuse, experiencing a negative life event, prior depressive episodes, history of cerebrovascular disease or heart disease, chronic pain, and a diagnosis of diabetes mellitus. Other issues often coexisting with late-life depression include multiple comorbidities, disability, and cognitive impairment. Common social stressors of the elderly may include loss of spouse, forced relocation (e.g., being forced to move in with family or assisted-living or nursing home placement), and retirement, which may lead to decreased self-worth, boredom, and loss of income.

Elderly depressed patients often complain of decreased concentration and show deficits in mental processing speed and executive function. These deficits often improve after treatment of depression (and are sometimes referred to as pseudodementia), but evidence suggests mild cognitive dysfunction does not always resolve completely. In fact, individuals who develop late-life depression and cognitive impairment have a higher risk of developing true dementia. Compared to younger adults, elderly patients with depression are less likely to report crying spells, sadness, or feeling like a failure. However, they are more likely to report poor appetite, experience irritability and withdrawal, and present to their health provider complaining of somatic complaints, such as vague aches and pains. This can lead to a delayed diagnosis and treatment, because providers are often focused on treating the physical complaints of the patient.

KEY POINT: There is a correlation with late-life depression and later-onset dementia. However, it is still unclear whether depression is a definitive risk factor for dementia or a prodromal symptom of dementia.

Suicide Risk

Age is a major risk factor for suicide. Suicidal ideation appears to occur more frequently in younger adults, but completed suicides are highest among older men. The use of a firearm is the most common method of death for elderly suicide patients. Risk factors for suicidal behavior in older adults include a coexisting psychiatric disorder especially anxious depression, substance abuse, a coexisting personality disorder, chronic medical illness, poor coping mechanisms, loneliness/isolation, and functional impairment.

Data suggest antidepressant medications may increase the risk of suicidal ideation in adolescents and young adults. However, this risk has not been observed in older adults. In fact, data suggest antidepressants may have a protective effect against suicidal ideation in the older population.

Summary of Standard Treatment in the Adult Population

When depression is suspected, the duration and severity of symptoms should be assessed and a treatment history addressing current and past therapies (nonpharmacologic and pharmacologic) should be performed. A physical examination, laboratory tests, and a thorough medical history should be obtained in order to assess whether medical conditions or medications may be worsening depressive symptoms (Table 13-1).

Symptom remission rather than simply response should be the optimal goal for clinicians and their patients. The large, multicenter STAR-D (Sequenced Treatment Alternatives to Relieve Depression) study showed patients who
Table 13-1. Medical Conditions and Medications Associated with Depression, Anxiety, and Insomnia

<table>
<thead>
<tr>
<th>Medical Conditions</th>
<th>Medications</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Depression</strong></td>
<td></td>
</tr>
<tr>
<td>B12 deficiency</td>
<td>Anticonvulsants</td>
</tr>
<tr>
<td>Cerebrovascular disease</td>
<td>Benzodiazepines</td>
</tr>
<tr>
<td>Chronic pain</td>
<td>Beta blockers</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>Clomipramine</td>
</tr>
<tr>
<td>HIV/AIDS</td>
<td>Cimetidine</td>
</tr>
<tr>
<td>Malignant disease</td>
<td>Clonidine</td>
</tr>
<tr>
<td>Malnutrition</td>
<td>Hydralazine</td>
</tr>
<tr>
<td>Multiple sclerosis</td>
<td>Opioid analgesics</td>
</tr>
<tr>
<td>Myocardial infarction</td>
<td>Steroids</td>
</tr>
<tr>
<td>Parkinson disease</td>
<td>Tamoxifen</td>
</tr>
<tr>
<td>Thyroid disorders</td>
<td></td>
</tr>
<tr>
<td><strong>Anxiety</strong></td>
<td></td>
</tr>
<tr>
<td>Angina</td>
<td>Alcohol withdrawal</td>
</tr>
<tr>
<td>Arrhythmias</td>
<td>Anticholinergics</td>
</tr>
<tr>
<td>Chronic obstructive pulmonary disease</td>
<td>Antidepressants (initiation of therapy)</td>
</tr>
<tr>
<td>Heart failure</td>
<td>Benzodiazepine withdrawal</td>
</tr>
<tr>
<td>Hyperthyroidism</td>
<td>Caffeine</td>
</tr>
<tr>
<td>Parkinson disease</td>
<td>Steroids</td>
</tr>
<tr>
<td>Pulmonary embolism</td>
<td>Sympathomimetics</td>
</tr>
<tr>
<td>Stroke</td>
<td>Theophylline</td>
</tr>
<tr>
<td><strong>Insomnia</strong></td>
<td>Thyroid hormones</td>
</tr>
<tr>
<td>Benign prostatic hyperplasia</td>
<td></td>
</tr>
<tr>
<td>Cardiovascular disease</td>
<td>Alcohol</td>
</tr>
<tr>
<td>Congestive heart failure</td>
<td>Anticholinergics</td>
</tr>
<tr>
<td>Chronic obstructive pulmonary disease</td>
<td>Antidepressants</td>
</tr>
<tr>
<td>Chronic pain</td>
<td>Antihistamines</td>
</tr>
<tr>
<td>Depression</td>
<td>Benzodiazepines</td>
</tr>
<tr>
<td>Malignancy</td>
<td>Beta agonists</td>
</tr>
<tr>
<td>Parkinson disease</td>
<td>Corticosteroids</td>
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<tr>
<td>Restless leg syndrome</td>
<td>Decongestants</td>
</tr>
<tr>
<td>Sleep apnea</td>
<td>Diuretics</td>
</tr>
<tr>
<td>Stroke</td>
<td>Nicotine</td>
</tr>
<tr>
<td>Thyroid disease</td>
<td>Xanthines</td>
</tr>
</tbody>
</table>

achieved remission were more likely to have increased daily function and less risk of relapse in the long term compared to those who only achieved a response with treatment. \(^{32}\)

Psychotherapy should be discussed as a treatment option, and patients should also be aware that it can often be used without drug therapy for mild depression. According to recent treatment guidelines, \(^{31}\) any second-generation antidepressant (selective serotonin reuptake inhibitor [SSRI], serotonin–norepinephrine reuptake inhibitor [SNRI], bupropion, or mirtazapine) can be used as a first-line agent when drug treatment is needed. If a response is seen after 4 to 6 weeks of therapy and the patient is tolerating the medication, then therapy should be continued. If only a partial response is observed, then the current antidepressant dose should be increased further or an additional agent added for augmentation. Recommended agents for augmentation...
include another second-generation antidepressant that has a different mechanism of action, thyroid hormone (T3 or T4), lithium, or a second-generation antipsychotic. In cases where no response is seen with the first-line agent, then the patient should switch to another antidepressant. When switching agents, cross-tapering is recommended.

Using the results from the STAR-D study as reference, clinicians can assume 30% of patients are likely to achieve remission (~50% will have a response) after taking one antidepressant for 12 weeks.32 For patients who move on to a level 2 treatment (augmentation agent or switching antidepressants), approximately 20% more will obtain remission. For resistant patients, third- and fourth-round treatments can be beneficial but achieving remission continues to be difficult.32

After remission has been achieved, treatment should continue for at least 6–9 months. Long-term therapy is recommended for patients who have had multiple episodes of depression in order to decrease the chance for recurrence.31

**Review of Evidence Supporting Treatment Recommendations for Geriatric Patients**

Evidence-based treatment options for depression in elderly patients also include psychotherapy and antidepressant medications. Medications are frequently prescribed in both the outpatient and institutionalized setting. However, psychotherapy has been shown to have equivalent efficacy compared to antidepressants in older adults, with 45% to 70% having clinical improvement.33 Combination therapy (both psychotherapy and antidepressant therapy) is most efficacious for severe or chronic depression.34,35

For mild depression, either psychotherapy alone or medication therapy alone can be used for treatment.36 Methods of psychotherapy that have shown clinical efficacy in late-life depression include cognitive behavioral therapy, interpersonal psychotherapy, supportive therapy, and problem-solving therapy.36 Therapy is usually provided for at least 6 to 12 treatments and is highly recommended for patients refusing pharmacologic treatment or for those who have not responded or only partially responded to drug therapy.37

When depression is assessed as moderate, medication treatment is strongly recommended, with or without psychotherapy. Combination therapy is recommended for severe or chronic depression.36

To date there have been several positive studies supporting SSRI and SNRI therapy for treatment of late-life depression.38-48 The mean age of patients in these studies ranged from 67 to 75 years, and rates ranged from 35% to 89% for response and 31% to 72% for remission. These agents appear to be as efficacious in the elderly as first-generation agents, such as tricyclic antidepressants (TCAs),29 but they are associated with fewer adverse effects and are safer in overdose situations.10,49,50 SSRI and SNRI antidepressants, along with mirtazapine and bupropion, are recommended as first-line agents for elderly patients according to the most recent treatment guidelines.36 When initiating antidepressant treatment, a low dose should be started but therapy should continue to be titrated to a moderate dose to receive an adequate response.36 A recent meta-analysis addressing antidepressant efficacy showed medication response is most likely to be observed after 10–12 weeks of therapy (versus 6 weeks in younger adults).50 However, literature also suggests approximately two-thirds of patients who do respond to antidepressants are likely to report partial improvement after 4 weeks of therapy.51

The initial antidepressant should be switched with another second-generation antidepressant (SSRI, SNRI, mirtazapine, or bupropion) if improvement is not seen with 4 weeks of a maximum tolerated dose or a partial response is not obtained with 8 weeks of a maximum tolerated dose.36 If a partial response is observed after 8–12 weeks, then augmentation with psychotherapy or with an additional agent is recommended.36

Lithium augmentation is the most studied strategy in the older population, demonstrating
an overall response rate of 42% when added to antidepressant therapy. However, this medication must be used cautiously because of the risk of toxicity, caused mainly by age-related decline in glomerular filtration. Other augmentation strategies that have been studied in the elderly include adding a different class of antidepressant (response rate = 31% to 45%) or adding a second-generation antipsychotic (response rate = 33% to 50%).

Studies have suggested that older adults are more likely to relapse or have a recurrence of depression sooner after adequate treatment compared to younger adults. Therefore, maintenance therapy should continue for at least 1–2 years after remission is achieved.

Electroconvulsive Therapy

A number of studies have shown electroconvulsive therapy (ECT) to be effective in late-life depression, with efficacy rates ranging from 60% to 80%. This treatment is indicated for treatment-resistant depression or for patients at high risk of serious harm because of psychotic depression or suicidal ideation. ECT is usually administered three times weekly for 2–6 weeks (total of 6–12 treatments) in an inpatient psychiatric setting, which limits its utilization. Common adverse effects include headache, temporary amnesia, and cognitive impairment. Permanent memory loss of the events surrounding the ECT treatments is a rare event but can occur. After ECT treatment is completed, maintenance therapy with an antidepressant medication is recommended to decrease the risk of relapse.

Common Problems Encountered When Treating Elderly Patients

Selective Serotonin Reuptake Inhibitors

Overall, SSRIs do not antagonize muscarinic, histaminic, or adrenergic receptors. Therefore, the common adverse effects observed with TCAs and monoamine oxidase inhibitors are not usually a concern with most SSRIs. The exception is paroxetine, which has moderate antimuscarinic activity—one reason it is not recommended as a first-line SSRI for the elderly. Compared to TCAs, cardiotoxicity is rare with SSRIs. However, a recent Food and Drug Administration (FDA) warning regarding citalopram was published in 2011 recommending lower dosing of citalopram (20 mg or less) in the elderly because of increased risk of prolonged QTc interval. Common adverse effects associated with SSRIs are due to increased activity at serotonin receptors. Gastrointestinal (GI) symptoms such as nausea, vomiting, and diarrhea are frequently noted. SSRIs are also associated with sexual dysfunction, appetite suppression, and sleep changes (both hypersomnia and insomnia). Fluoxetine is associated with more anxiety and agitation compared to other SSRIs. Because of these adverse effects and its long half-life, fluoxetine is not considered a first-line SSRI for older adults.

There are particular SSRI adverse effects more prevalent in the elderly than in younger adults. These include hyponatremia, extrapyramidal adverse effects, and increased bleeding. SSRI-induced hyponatremia occurs in 10% to 15% of older adults and is more common in women. Paroxetine appears to have the highest incidence within this class. The hyponatremia is likely the result of increased secretion of antidiuretic hormone. Extrapyramidal side effects such as parkinsonism, dystonia, and akathisia are observed in 10% of older adults taking SSRI therapy. These effects are possibly due to decreased nigrostriatal dopaminergic transmission indirectly caused by increased serotonin activity. Bleeding risk appears to be higher in elderly patients who take SSRIs compared to younger adults. GI bleed risk is increased when these agents are taken concurrently with nonsteroidal anti-inflammatory drugs. Bleeding risk is possibly due to SSRIs preventing platelet reuptake of serotonin, resulting in decreased platelet action. Bleeding risk should be assessed and monitored closely, especially for patients taking antiplatelets and anticoagulants concurrently with SSRI therapy.

All SSRIs are metabolized by cytochrome P450 enzymes. Paroxetine significantly inhibits 2D6 isoenzymes, whereas fluoxetine inhibits
2D6, 3A4, and 1A2, making these two agents more likely to interact with other medications. Sertraline weakly inhibits 2D6 at higher doses, and citalopram and escitalopram have very little inhibition activity, making these three agents the preferred ones for elderly patients taking multiple medications.

Serotonin and Norepinephrine Reuptake Inhibitors

Venlafaxine, desvenlafaxine, and duloxetine result in increased levels of serotonin and norepinephrine in the synaptic cleft by inhibiting the reuptake of these neurotransmitters back into the presynaptic neuron. Patients who fail to respond to SSRIs may find efficacy with SNRIs because of the dual neurotransmitter effect. These agents may also be beneficial for patients with concurrent neuropathic pain or fibromyalgia. Studies have shown venlafaxine and duloxetine to be efficacious and well-tolerated in the elderly, although one trial did suggest that venlafaxine may be less well tolerated in the frail elderly compared to SSRIs.

Serotonergic adverse effects such as GI upset, sexual dysfunction, and sleep changes are commonly observed with SNRIs. Cases of hyponatremia have also been noted with venlafaxine use. SNRIs should typically be given in the morning because of the risk of insomnia if given at bedtime. These agents are also associated with elevated blood pressure at high doses (risk is greater for venlafaxine versus duloxetine); therefore, blood pressure should be monitored regularly with therapy.

Both venlafaxine and duloxetine are metabolized by the cytochrome P450 isoenzymes. Venlafaxine has very weak inhibition, and duloxetine has moderate inhibition at the 2D6 pathway. However, these effects have not been shown to be clinically significant in most cases. Desvenlafaxine is an active metabolite of venlafaxine. It has minimal P450 metabolism, and 45% of the drug is excreted unchanged in the urine. Therefore, lower dosing is recommended for patients with reduced renal function. Overall, SNRIs can be used in older patients taking multiple medications without cause of concern, although dosage recommendations should follow the standard recommendation in older adults to “start low and go slow, but go.”

Bupropion and Mirtazapine

Bupropion inhibits the reuptake of dopamine and norepinephrine in the central nervous system (CNS), causing an increase in these neurotransmitters in the neuronal synaptic cleft. Because of bupropion’s mechanism of action, it is the most activating agent compared to other antidepressants. Doses should not be taken at night because of the risk of insomnia. There are limited data on use of bupropion in the elderly, but according to treatment guidelines it can be considered as a first-line therapy. Bupropion may be useful for depression associated with apathy, lack of motivation, and hypersomnia, and data suggest it may have a role in augmentation therapy when used in treatment-resistant depression.

Common adverse effects of bupropion include tremors, nervousness, and elevated blood pressure and pulse. Bupropion is contraindicated in patients with a history of seizures and should not be used in patients with anxiety disorders. Compared to other antidepressants, bupropion is most likely to cause appetite suppression and weight loss and, therefore, should be used cautiously in elderly patients who have decreased oral intake. When using the medication, blood pressure and pulse should be monitored regularly.

Mirtazapine acts as a central alpha antagonist, resulting in increased release of serotonin and norepinephrine in the CNS. This agent is also a potent antagonist of histamine receptors and, therefore, causes sedation and increased appetite. Compared to the quantity of SSRI and SNRI data, there is significantly less published information regarding the efficacy of mirtazapine in late-life depression. However, small studies do suggest mirtazapine is as effective as other first-line therapies and may be useful for depressed elderly who also have decreased oral intake or insomnia.
Tricyclic Antidepressants

In general, TCAs work similarly to SNRIs by inhibiting the reuptake of both serotonin and norepinephrine. However, each tricyclic agent has varying degrees of potency on the reuptake transporters, making some agents more serotonergic and others more noradrenergic in action. TCAs are effective but less well tolerated in older adults compared to SSRIs and SNRIs. These agents also inhibit cardiac sodium-potassium adenosine triphosphatase (Na/K ATPase) pump and act as antagonists at alpha, muscarinic, and histaminic receptors, which can lead to significant adverse effects. TCAs can worsen symptoms of chronic conditions such as benign prostate hyperplasia, urinary retention, constipation, cognitive impairment, glaucoma, orthostatic hypotension, cardiac disease, and arrhythmias.

Secondary amines such as nortriptyline and desipramine are associated with less anticholinergic, antihistaminic, and orthostatic hypotension compared to the tertiary amines. However, cardiac toxicity is equal among both groups of drugs. Compared to the other classes of antidepressants, TCAs are more likely to be fatal on overdose. Even though TCAs have been proven to be efficacious for late-life depression, they should not be used as first-line therapy because of the high risk of adverse effects. If tricyclic therapy is necessary, then nortriptyline is usually recommended, as it has data to support its efficacy as monotherapy and as an augmentation agent for patients who fail SSRI therapy. Drug levels should be obtained and monitored. A concentration of 80–120 ng/mL is the goal range for efficacy and safety.

KEY POINT: The benefits of using SSRI therapy as a first-line agent for late-life depression outweigh the risks. However, geriatric patients are at higher risk of developing hyponatremia, extrapyramidal adverse effects, and GI bleeding with SSRI therapy compared to younger adults.

Anxiety

Etiology, Epidemiology, and Clinical Presentation Specific to Geriatrics

Compared to late-life depression, fewer studies exist and less is known about the presentation, treatment, and prognosis of late-life anxiety disorders. The most recent epidemiologic data found the prevalence rates of late-life anxiety disorders to be around 7% within a recent 12-month period and 15% for lifetime occurrence. Research shows that anxiety disorders are common in late life; however, they appear to be less prevalent in older adults compared to younger adults. These results may certainly be true, but it is suspected that many cases of late-life anxiety are not being detected properly or symptoms are being misdiagnosed.

Comorbid anxiety and depression are observed three times more often than pure anxiety. The prevalence of older adults with anxiety who also suffer from major depressive disorder ranges from 13% to 30%. Elderly patients with both depression and GAD are more likely to have severe, chronic depressive symptoms and suicidal ideation compared to those suffering only from depression. In addition, older adults suffering from any anxiety disorder with depression have lower social functioning and require increased health services compared to elderly patients with pure anxiety.

Anxiety disorders is a broad term that includes multiple individual disorders such as GAD, panic disorder, specific phobias, social anxiety disorder, obsessive-compulsive disorder (OCD), acute stress disorder, and post-traumatic stress disorder (PTSD). In the recently published DSM-5 text, OCD was moved from Anxiety Disorders to a new chapter entitled “Obsessive-Compulsive and Related Disorders,” and PTSD was moved to “Trauma and Stressor-Related Disorders.” The most common anxiety diagnoses observed in older adults are GAD and specific...
phobias. Table 13-2 provides an overview of the diagnostic criteria for each anxiety disorder and its prevalence in the geriatric population.

Limitations in Identifying Anxiety Disorders, Risk Factors, and Presentation Specific to Geriatric Patients

Data from the National Comorbidity Survey Replication study showed that less than 1% of the population developed a newly diagnosed anxiety disorder after 65 years of age, demonstrating that most late-life anxieties likely developed in early adulthood and persisted through the older years. However, GAD appears to be the exception. Episodes of late-life GAD are found to be an even combination of chronic patients who report having anxiety symptoms since early adulthood and patients whose symptoms started in late life.

Noted risk factors are female sex, having medical comorbidities, being single or divorced, lower education, low subjective health, stressful life events, limitations with daily activities, and neuroticism. Older adults with late-life anxiety often present to their primary care provider complaining of unexplained physical symptoms such as fatigue, aches, pains, GI symptoms, or trouble sleeping, which may result in a delay of the correct diagnosis.

As stated earlier, it is suspected that late-life anxiety may be underdiagnosed. Detection and diagnosis of late-life anxiety can be complicated by patients’ medical comorbidities, decreased cognition, and changes in life circumstances. Specific factors that may contribute to poor screening and diagnosis include (1) clinicians and patients assuming anxiety and avoidance behaviors are normal with aging, (2) patients minimizing their emotional symptoms, (3) patients attributing their anxiety symptoms to physical illnesses, (4) patients’ difficulty remembering their symptoms, and (5) older adults experiencing more fear or worry about different situations than younger adults.

KEY POINT: There is a high prevalence of comorbid depression with late-life anxiety. Patients who meet diagnostic criteria for anxiety should also be screened for major depressive disorder.

Summary of Standard Treatment in the Adult Population

Goals of treatment for all patients with anxiety disorders include decreasing anxiety severity, improving level of function, and obtaining remission. For acute treatment, benzodiazepines are the only pharmacologic treatment available with a quick onset of action. They may also need to be used for chronic treatment for patients who obtain only a partial response with antidepressants. Guidelines recommend SSRIs and SNRIs as first-line agents for the chronic treatment of most anxiety disorders. If first-line agents are ineffective, then TCAs can be tried. Buspirone can also be considered as a second- or third-line agent for chronic treatment of GAD. After an adequate response is achieved, treatment should generally continue for at least 12 months. Long-term therapy is recommended for patients with multiple episodes of anxiety. Cognitive-behavioral therapy (CBT) has been shown to be equally efficacious for treatment of anxiety disorders compared to pharmacotherapy for younger adults and, if available, patients may choose this option over drug therapy.

Review of Evidence Supporting Treatment Recommendations for Geriatric Patients

Psychotherapy

Although drug therapy is often recommended for late-life anxiety, psychotherapy may also be efficacious and preferred for older adults who are sensitive to medication adverse effects or trying to avoid polypharmacy. CBT is the most studied psychotherapy in older adults with anxiety and may include breathing retraining, muscle relaxation, cognitive restructuring to focus on the
### Table 13-2. Diagnostic Criteria and Prevalence of Anxiety Disorders

<table>
<thead>
<tr>
<th>Disorder</th>
<th>Diagnostic Criteria Description</th>
<th>U.S. Prevalence in Older Adults</th>
</tr>
</thead>
<tbody>
<tr>
<td>Generalized anxiety disorder</td>
<td>Anxiety and worry that is difficult to control, occurs most days for at least 6 months, and leads to impairment of daily function. The anxiety and worry are also associated with at least three of the following: restlessness, easily fatigued, trouble concentrating, irritability, muscle tension, sleep disturbances. The symptoms are not substance-induced or due to another medical/mental disorder.</td>
<td>1.2%</td>
</tr>
<tr>
<td>Panic disorder</td>
<td>Recurrent panic attacks; symptoms present abruptly and peak within minutes, including (must have four or more): heart palpitations, sweating, trembling, shortness of breath, feelings of choking, chest pain, nausea, dizziness, chills or heat sensations, paresthesias, depersonalization, fear of losing control, fear of dying. After an attack occurs, individual (1) continues to worry about having another attack and/or (2) avoids situations/places because of the fear of having another attack. The symptoms are not substance-induced or due to another medical/mental disorder.</td>
<td>0.7%</td>
</tr>
<tr>
<td>Social anxiety disorder</td>
<td>Fear or anxiety about social situations in which the individual could be scrutinized by others. The individual fears that he or she will act in a way that will be negatively observed by others. Social situations almost always lead to fear or anxiety, and the fear is greater than the actual threat of the social situation. Social situations are often avoided. Fear, anxiety, or avoidance persists for 6 months or more and causes impairment in daily function. The symptoms are not substance-induced or due to another medical/mental disorder.</td>
<td>2% to 5%</td>
</tr>
<tr>
<td>Diagnostic Criteria</td>
<td>Description</td>
<td>U.S. Prevalence in Older Adults</td>
</tr>
<tr>
<td>---------------------</td>
<td>-------------</td>
<td>-------------------------------</td>
</tr>
<tr>
<td><strong>Specific phobias</strong></td>
<td>Fear or anxiety about a specific object or situation &lt;br&gt;The phobia almost always leads to fear or anxiety, and the fear is greater than the actual threat of the specific object or situation &lt;br&gt;The phobic object or situation is often avoided &lt;br&gt;Fear, anxiety, or avoidance persists for 6 months or more and causes impairment in daily function &lt;br&gt;The symptoms are not substance-induced or due to another medical/mental disorder</td>
<td>3% to 5%</td>
</tr>
<tr>
<td><strong>Posttraumatic stress disorder</strong>&lt;sup&gt;a&lt;/sup&gt;</td>
<td>Exposure to a traumatic event (threat of or actual death or serious injury) &lt;br&gt;Experiences symptoms from all four cluster of symptoms: &lt;ul&gt;&lt;li&gt;Re-experiencing (e.g., flashbacks, nightmares, dissociative behavior)&lt;/li&gt;&lt;li&gt;Avoidance&lt;/li&gt;&lt;li&gt;Numbing (e.g., detachment from others, restricted affect, cannot remember the details of the traumatic event)&lt;/li&gt;&lt;li&gt;Increased arousal (e.g., insomnia, hypervigilance, increased startle response)&lt;/li&gt;&lt;/ul&gt;Duration of symptoms is 1 month or longer &lt;br&gt;The symptoms cause impairment in daily function</td>
<td>0.4%</td>
</tr>
<tr>
<td><strong>Obsessive-compulsive disorder</strong>&lt;sup&gt;b&lt;/sup&gt;</td>
<td>Obsessions, compulsions, or both are present &lt;ul&gt;&lt;li&gt;Obsessions: &lt;ul&gt;&lt;li&gt;Thoughts that are intrusive, inappropriate, and cause significant distress&lt;/li&gt;&lt;li&gt;Attempts are made to suppress or eliminate the thoughts&lt;/li&gt;&lt;/ul&gt;&lt;/li&gt;&lt;li&gt;Compulsions: &lt;ul&gt;&lt;li&gt;Repetitive behaviors performed by the person in response to the obsession&lt;/li&gt;&lt;li&gt;Behaviors are not pleasurable but are performed to prevent discomfort or a negative event&lt;/li&gt;&lt;/ul&gt;&lt;/li&gt;&lt;/ul&gt;The symptoms cause distress, are time consuming, or impair daily function &lt;br&gt;The symptoms are not substance-induced or due to another medical/mental disorder</td>
<td>0.7%</td>
</tr>
</tbody>
</table>

<sup>a</sup>DSM-5 now classifies the disorder under Trauma and Stressor-Related Disorders.<br>
<sup>b</sup>DSM-5 now classifies the disorder under Obsessive-Compulsive and Related Disorders.
consistent worrying, and graded exposure so the patient can learn how to cope in stressful/ phobic situations.\textsuperscript{75} Study results regarding the efficacy of CBT for anxious elderly patients conflict. Some studies have suggested that CBT therapy may be less efficacious for older than for younger adults with anxiety.\textsuperscript{85-87} However, at least three meta-analyses have concluded that CBT significantly reduced anxiety symptoms for older adults compared to the active control groups.\textsuperscript{88-90} A recent study also found CBT to be effective in reducing relapse of anxiety symptoms, similar to SSRI therapy but better than placebo.\textsuperscript{91}

Most CBT studies in the elderly focus on treating GAD, so there are less data addressing the treatment of other anxiety disorders.\textsuperscript{92} Much of the CBT research often excludes sicker elderly, the cognitively impaired, and patients older than 75. However, a limited number of studies have been done to assess efficacy in these populations.\textsuperscript{93-95} It has been suggested that CBT should be modified for older adults. Recommended modifications include using group therapy versus individual therapy, providing more emphasis on increasing the motivation of patients, using learning and memory aids during discussions, and providing the patients weekly calls to check for questions or problems relating to the therapy session homework assignments.\textsuperscript{91,96}

**Antidepressants**

Many of the SSRIs and SNRIs are FDA labeled for anxiety disorders and considered first-line treatment for chronic management of anxiety in adults. There are limited data addressing these antidepressants and their efficacy in late-life anxiety, but they are still commonly prescribed by geriatric clinicians because of their low risk of serious adverse effects.\textsuperscript{69} Agents that have clinical data supporting their use in the elderly with anxiety disorders include citalopram,\textsuperscript{97,98} sertraline,\textsuperscript{99} escitalopram,\textsuperscript{91} duloxetine,\textsuperscript{100} and venlafaxine,\textsuperscript{101} although the other SSRIs and mirtazapine have proven effective in younger adults.

Lenze and colleagues lead a randomized, placebo-controlled study of citalopram for the treatment of anxiety disorders in the elderly.\textsuperscript{57} Diagnoses of the patients included GAD, panic disorder, and PTSD, although a great majority of the patients were diagnosed with GAD. Sixty-five percent of patients assigned to citalopram treatment (dose = 20–30 mg/day) achieved a response by 8 weeks, whereas only 24% in the placebo responded.

After 8 weeks of treatment, the study patients were eligible to continue an open-label study of citalopram for 24 more weeks. Patients who responded to citalopram during the first 8 weeks continued to take citalopram, and individuals who failed to respond with placebo were switched to citalopram for the rest of the long-term study. Those who were taking citalopram and did not respond during the first 8 weeks were omitted from the long-term study. Blank and colleagues\textsuperscript{98} published the results of the long-term study and found anxiety rating scale scores continued to improve throughout the study; 60% were responders at the end of the study.

Sertraline was compared to CBT and placebo for treatment of late-life anxiety in a 3-month study lead by Schuurmans and colleagues.\textsuperscript{99} The average age of the participants was 70, and their diagnoses included GAD, panic disorder, agoraphobia, and social phobia. Patients taking sertraline at a maximum dose of 150 mg/day showed statistically significant improvement in anxiety and depressive symptoms compared to the waitlist controls. Sertraline also showed to be better than CBT for worry during the length of the study.

In a 2009 study performed by Lenze and colleagues,\textsuperscript{102} escitalopram 10–20 mg was not more effective than placebo for treatment of GAD after an intent-to-treat analysis. However, a more recent study\textsuperscript{91} did show escitalopram to improve symptoms on the Hamilton Rating Scale for Anxiety (HRSA) when used as monotherapy and when combined with CBT. Continuation of escitalopram also decreased the risk of relapse compared to placebo.

The clinical effects and tolerability of duloxetine in the elderly were investigated by Davidson...
and colleagues. The authors reviewed four previous duloxetine studies and performed a subgroup analysis for the older adults who were enrolled (73 patients). Overall, patients assigned to duloxetine had greater improvement on anxiety and depression scales compared to the placebo group after 9–10 weeks of therapy. However, it was noted that 22% stopped therapy due to adverse effects, with nausea and weight loss being the most common.

Katz and colleagues investigated the efficacy and tolerability of venlafaxine extended-release for treatment of GAD in elderly patients. The researchers performed a retrospective review of data from five randomized placebo-controlled trials. Data pertaining to the older adults (≥60 years of age) enrolled in the studies were collected. All five studies were at least 8 weeks in duration and two of them continued through 24 weeks. Overall, the researchers found that assessment score changes from baseline to follow-up for the intention-to-treat group were not significantly different compared to placebo. One assessment score, the Clinical Global Impression of Improvement (CGI-I), was the only score that significantly improved among the venlafaxine group compared to placebo. Remission and response rates were noted as secondary objectives. For the intention-to-treat group, response rates were significantly higher according to the CGI-I scale for patients taking venlafaxine at both weeks 8 and 24. Venlafaxine was found to cause more GI adverse effects compared to the placebo group, but the overall discontinuation rates were not significantly different.

The authors also noted the outcomes for the younger population (<60 years of age). Interestingly, patients taking venlafaxine had more improvement compared to the placebo group according to all assessment reports. Also, the younger patients taking venlafaxine continued to have significantly higher response and remission rates through weeks 8 and 24. These results suggest that a better response to venlafaxine is observed in younger adults compared to older adults. However, one should keep in mind the number of geriatric patients may not have been high enough to meet the power requirement of the study.

Antidepressants need to be taken at a therapeutic dose for 6 weeks before a response will be seen. Initially, these agents may appear to worsen anxiety symptoms by causing jitteriness and activation. Counseling the patient on these transient adverse effects ahead of time is recommended, along with frequent follow-up during the first 2 months of therapy. Also, initiating therapy at a low dose and titrating carefully can decrease the severity of adverse effects. Additional information regarding which SSRIs are better in the elderly and common adverse effects were discussed previously (see Depression).

Benzodiazepines

Benzodiazepines have a rapid onset of action and are currently the only option for acute treatment of anxiety symptoms. These agents are efficacious but can cause significant adverse effects such as excessive sedation, depressed mood, cognitive impairment, tolerance and dependence, amnesia, unstable gait, increase risk for falls, and respiratory depression. Severe withdrawal symptoms such as seizures and exacerbation of anxiety can occur if these agents are stopped suddenly or tapered too quickly. Because the risk of benzodiazepines often outweighs their benefit in the elderly population, they are generally not recommended for long-term use. However, a recent study found that more than 50% of older adults with anxiety disorders were using a benzodiazepine at baseline and use did not decline over a 9-year period, suggesting this drug class is still overused.

If a benzodiazepine is needed, lorazepam and oxazepam are the preferred agents because of their short half-life, no active metabolite, and lack of CYP450 involvement. Patients who have been on benzodiazepine therapy for many years may find it difficult to taper off because of worsening anxiety symptoms. In this case, if the medication is not causing significant adverse effects, it may be better for the patient...
to continue it while trying to use the lowest dose possible to control symptoms.75

**KEY POINT:** Generally, the risks of chronic benzodiazepine use outweigh the benefits. However, older patients who have been taking the drug for years find it difficult to discontinue therapy (even with gradual tapering) without anxiety symptoms recurring.

### Buspirone

Buspirone works as a partial agonist at the 5-HT\textsubscript{1A} receptors. Although the medication is efficacious for GAD, it is not a recommended therapy for other anxiety disorders.83 Buspirone is not associated with dependence, sedation, depressed respiratory rate, or psychomotor impairment, as seen with benzodiazepine therapy. Studies have shown buspirone to be effective and well tolerated in the geriatric population.105-107 However, the therapeutic response is less predictable compared to the antidepressants and benzodiazepines. Clinicians must remember buspirone is not quick acting and can take up to 2–3 weeks before an effect is observed. The twice to three times a day dosing schedule can often be a burden for elderly who have multiple medications to organize.69,75 Also, buspirone has been shown to be less efficacious for those who have chronically used benzodiazepines in the past.108 For treatment of GAD, buspirone is considered a second- or third-line agent for chronic management, falling behind antidepressants.84 If used, the recommended starting dose in older adults is 5 mg twice daily. It can be increased by 5 mg every 4–5 days to a target dose of 20–30 mg/day given in divided doses.75

### Common Problems Encountered When Treating Elderly Patients

Due to the lack of data in older adults, much of the treatment guidelines are extrapolated from data obtained from younger adults.69,75 When anxiety is suspected, a thorough history of the illness should be obtained, including current and past symptoms, history of medications used, family history of mental illness, and history of substance abuse. Along with a mental status examination, a physical examination with laboratory values should be performed. A full medical history will help decide whether physical factors or medications are contributing to a patient’s anxiety (Table 13-1).

Because of the high prevalence of psychiatric comorbidity, elderly patients who screen positive for an anxiety disorder should also be assessed for depression.75 For patients who meet diagnostic criteria for both major depressive disorder and GAD, a separate diagnosis of GAD is not needed unless it is clear the patient has experienced GAD symptoms outside the depressive episodes.75

CBT can be used as monotherapy or in combination with medications for treatment of anxiety disorders, but, as mentioned previously, CBT may need to be modified to meet the needs of older adults.92 SSRIs and SNRIs are both considered first-line medication therapies for long-term treatment of anxiety disorders. However, according to the published data, SNRIs may be more likely to cause adverse effects.100,101 Doses of the agents should be started low but continue to be titrated to therapeutic doses. If a patient does not respond to the first-line agent after 6 weeks of therapy, switching to a different class of antidepressant (i.e., switch from an SSRI to a SNRI, or vice versa) is recommended.75

Because antidepressants take several weeks to induce a response, short-term benzodiazepine use is indicated if the patient needs acute treatment. An antidepressant should be started with the benzodiazepine, and the purpose of each, along with the expected outcome, should be explained to the patient. After 6 weeks of combination therapy, a tapering schedule for the benzodiazepine should be initiated and eventually discontinued if possible.68,75 For patients who do not receive adequate anxiety relief with an antidepressant alone, long-term treatment with benzodiazepines may be necessary. In this case, the lowest dose possible
to treat symptoms should be used. Agents of choice for older adults include lorazepam (0.5–2 mg/day) and oxazepam (10–30 mg/day).75

After an adequate response is achieved, therapy should be continued for at least 1 year. Elderly with chronic recurrence of anxiety should continue treatment long term. If anxiety presents with major depressive disorder, then treatment duration should be decided by the patient’s depression history.75

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**Insomnia**

**Etiology, Epidemiology, and Clinical Presentation Specific to Geriatrics**

Insomnia is a condition that can affect patients at any age. It is often assumed that older patients require less sleep, especially because sleep complaints are common in the elderly population. However, insomnia is not a normal characteristic of aging and should be evaluated and treated appropriately.

Approximately 60% of community-dwelling elderly patients report some form of disruption of sleep, with difficulty falling asleep, nocturnal waking, and waking up too early being the most common complaints.109 When compared to the younger population (<60 years of age), older patients (>80 years of age) have more complaints regarding decreases in sleep quality, waking repeatedly during sleep, and having a difficult time getting back to sleep after waking up in the middle of the night.109,110

Sleep complaints, and the resulting daytime sleepiness, are associated with a significant impact on both community-dwelling and facility-dwelling elderly patients, including decreased quality of life, impaired cognition, more depressive symptoms, higher risk of frailty, lower functional status, decreased social interactions, and increased mortality.109,112-122

**Sleep Changes in the Elderly**

Brief (<30 seconds) nocturnal awakenings occur in patients of any age; aging is associated with an increased frequency and duration of these nocturnal awakenings.123 Sleep latency and the number of early morning awakenings increase with age. Total sleep time, sleep efficiency, and rapid eye movement (REM) sleep latency are also affected.111,123-126 From midlife until the ninth decade, total sleep time may decrease by an average of 27 minutes per decade.126 Changes in sleep architecture in the elderly are evident on polysomnography. Time spent in stages 1 and 2 increases, and time spent in stages 3 and 4 (“deep sleep”) and REM sleep decreases.111,123-125

Age-related changes in sleep maintenance and sleep architecture alter the homeostatic drive for sleep. Decreased sleep during nighttime hours increases the homeostatic drive for sleep during the day, resulting in daytime drowsiness and daytime napping. The increase in the frequency and duration of daytime naps causes the homeostatic drive for sleep to decrease on the subsequent night.123,125,126

The amplitude and the shifting (to an earlier time) of the circadian rhythm may result in sleepiness at earlier-than-usual times. Several studies have demonstrated that these changes are associated with poor sleep quality, altered sleep architecture, increased awakenings during sleep, early morning awakenings, and increased daytime sleepiness.124,125,127

Growth hormone and cortisol levels have been associated with sleep quality in healthy older men. In one study, growth hormone levels decreased by nearly 75% from young adulthood to midlife (fifth decade) and continued to decrease into late adulthood. Reduced amounts of shortwave/deep sleep were associated with reduced amounts of growth hormone secretion. Cortisol levels, specifically the evening nadir levels, were significantly increased from midlife to late life as compared to younger counterparts. This was associated with decreased amounts of REM sleep and increased amount of wake time.125,128
KEY POINT: Age-related changes in sleep architecture and physiology may result in decreased sleep maintenance and quality in the elderly patient.

Due to the decreased time spent in stages 3 and 4, elderly patients are more likely to awaken from noise in the environment. Residing in a long-term care facility is not conducive to promoting quality sleep because of night-time noise or light and room sharing. Long-term care residents are often in poor physical health as compared to their counterparts residing in the community, and this may impact their sleep quality.

Assessment of Insomnia in the Elderly

Many elderly patients do not discuss their sleep complaints with their healthcare provider. These patients tend to try interventions that may actually worsen sleep, such as watching TV, listening to the radio, reading, taking a nap, drinking alcohol, or smoking a cigarette. Healthcare providers should routinely ask older patients about their sleep habits and the treatments that have been tried.

The assessment of daytime functioning may be an appropriate clinical measure to evaluate the significance of insomnia on an individual patient. Negative impact on daytime functioning is stressed in the DSM-5 diagnostic criteria for insomnia disorder. Sleep disturbances in an elderly patient may adversely affect daytime functioning, including complaints of napping and not feeling well rested on awakening.

KEY POINT: Older patients should be routinely asked about their sleep habits and which treatments have been tried.

Sleep diaries or questionnaires are often used to assess sleep complaints. Some questions that may be helpful include asking patients what time they fall asleep at night and wake up in the morning, if they feel sleepy during the day, if they have difficulties falling asleep, how many times they wake up during the night, and if other symptoms are present while sleeping (e.g., snoring, leg discomfort, breathing difficulty, movements). Asking the spouse or caregiver these questions may also provide some insight for the clinician. The Pittsburgh Sleep Quality Index is a valid and reliable self-rated questionnaire that gathers information on sleep habits, daytime effects of sleep disorders, and etiology of nocturnal sleep disruption.

A thorough evaluation of the patient’s overall physical and psychological health and medication use should be performed. Multiple conditions affect the quality and quantity of sleep by impacting a patient’s pain/discomfort level, ability to breathe, ability to urinate, or general mental condition. Almost all diseases that are common in the elderly population can adversely affect sleep (see Table 13-1). When identifying these comorbid conditions, the clinician should consider if these diseases are appropriately treated or controlled before initiating pharmacologic therapy for insomnia.

Medications that cause stimulation, anxiety, increased urination, excessive drowsiness, or mental status changes should be evaluated. Some examples of medications that may cause these symptoms are found in Table 13-1. Many of these medications have specific negative effects on sleep staging and quality.

KEY POINT: Several comorbid conditions can adversely affect sleep. Before initiating pharmacologic therapy for insomnia, the clinician should evaluate if any comorbid conditions are appropriately treated or controlled.
Summary of Standard Treatment in the Adult Population

Education on proper sleep hygiene or cognitive behavioral therapy is typically provided when insomnia is diagnosed. When nonpharmacologic therapy is ineffective, a short course of a hypnotic agent is added. Hypnotic agents include sedating antihistamines, benzodiazepines, benzodiazepine-receptor agonists, doxepin, or ramelteon. Use of hypnotic agents should be at the lowest effective dose for the shortest duration possible.

Review of Evidence Supporting Treatment Recommendations for Geriatric Patients

Proper sleep hygiene addresses healthy lifestyle habits and environmental factors that influence sleep. Sleep hygiene alone is often insufficient to treat insomnia in an elderly patient. A variety of other nonpharmacologic therapies, such as relaxation, stimulus control, sleep restriction, and cognitive behavioral therapy can be beneficial for an elderly patient. Cognitive behavioral therapy and pharmacologic therapy in combination is more effective in the treatment of insomnia than either treatment approach alone. The use of cognitive behavioral therapy when drug therapy is discontinued maintains remission of insomnia, is preferred, and is perceived by patients to be effective.

Several studies have demonstrated that Tai Chi is effective in improving sleep quality and daytime sleepiness in elderly patients. Moderate exercise, consisting of 30–40 minutes of low-impact aerobics or brisk walking performed four times per week, has been shown to improve sleep quality, sleep latency, and sleep duration in patients between 50 and 76 years of age. Exercise should not be performed within an hour of bedtime. Decreasing or eliminating daytime napping may not be as beneficial as initially thought, as one study revealed that day or evening naps were not correlated with poor sleep characteristics (sleep latency, awakenings after sleep onset, impaired sleep efficiency) in older patients.

Older patients report that prescription hypnotic agents are effective in treating sleep difficulties. Several epidemiologic studies have shown that benzodiazepines are commonly prescribed in the elderly population. These agents reduce sleep latency, reduce the number of awakenings, and increase total sleep time. Although benzodiazepines have little or no effect on REM sleep, the duration of sleep stages 1 and 4 is decreased whereas the duration of sleep stage 2 is increased. The hypnotic benzodiazepines (estazolam, temazepam, triazolam, quazepam) are effective in treating insomnia and can be used in short courses (<14 days). However, due to the frequency of adverse effects that typically occur in an elderly patient with the use of these agents, they should be avoided as first-line treatment for insomnia. Benzodiazepines have been associated with worsening sleep complaints, increased falls, excessive daytime sleepiness, increased fractures, and motor vehicle crashes in elderly patients.

The benzodiazepine-receptor agonists (zolpidem, zaleplon, and eszopiclone) have been shown to be effective for the treatment for insomnia in the elderly population. These agents increase total sleep time, decrease the number of nocturnal awakenings, decrease sleep latency, and improve sleep quality. A meta-analysis has found that zolpidem, zaleplon, and eszopiclone have similar efficacy compared to benzodiazepines. Their effects on improving sleep onset and sleep maintenance enable these agents to target common sleep disturbances in an elderly patient. The benzodiazepine-receptor agonists cause minimal effects on tolerance, rebound insomnia, and residual daytime drowsiness. A meta-analysis has found that zolpidem, zaleplon, and eszopiclone have similar efficacy compared to benzodiazepines. Their effects on improving sleep onset and sleep maintenance enable these agents to target common sleep disturbances in an elderly patient. The benzodiazepine-receptor agonists cause minimal effects on tolerance, rebound insomnia, and residual daytime drowsiness. Recent data have shown that the benzodiazepine-receptor agonists may increase the risk of hip fracture, motor vehicle accidents, and may cause similar adverse effects (confusion, memory loss, falls) as the benzodiazepines.

Benzodiazepine-receptor agonists can cause complex sleep-related behaviors, such as sleep-driving, making phone calls, and...
preparing and eating food (while asleep), with subsequent amnesia of these behaviors. Patients should be counseled to take the medication immediately before going to bed, to avoid taking the medication with or immediately after a meal, and to alert the bed partner to watch for these behaviors so alternative treatment can be tried. These agents may also cause anaphylaxis and angioedema. As a result of postmarketing surveillance, labeling of these products is now required to state these potential effects.\textsuperscript{156}

In melatonin-deficient elderly patients, melatonin replacement is beneficial in improving sleep latency and sleep efficiency.\textsuperscript{157} Its use in patients who are not specifically deficient in this hormone is ineffective in treating primary insomnia.\textsuperscript{158,159} The melatonin-receptor agonist, ramelteon, has been proven to be effective in elderly patients with insomnia. Ramelteon improves self-reported sleep latency and total sleep time.\textsuperscript{160} Recent data indicate that ramelteon can impair driving performance.\textsuperscript{161} It carries the revised warning labeling regarding possible anaphylaxis and angioedema but, in general, is safer in elderly patients than the benzodiazepine-receptor agonists.\textsuperscript{156}

Doxepin causes sedation because of its high selectivity for the histamine-1 receptor. Low-dose doxepin is effective in increasing total sleep time, decreasing the number of nocturnal awakenings, and improving sleep quality and efficiency in elderly patients with insomnia. Low-dose doxepin (3- or 6-mg tablets) causes minimal effects on residual daytime drowsiness, rebound insomnia, and cognition and is not associated with complex sleep behaviors. Doxepin may cause anticholinergic adverse effects, such as constipation, xerostomia, or urinary retention; however, clinical trials for low-dose doxepin reported incidence rates comparable to placebo or no anticholinergic adverse effects.\textsuperscript{162-165}

### Common Problems Encountered When Treating Elderly Patients

Residual daytime drowsiness is a common phenomenon for geriatric patients because of the pharmacokinetic alterations in renal function, hepatic function, and volume of distribution that occur with aging. For this reason, the lowest doses are recommended, even for agents that are short acting. Extended-release agents may not be an optimal choice because of slowed motility of the GI tract in addition to the other altered pharmacokinetic parameters.

Common nonpharmacologic interventions for sleep difficulty used by older adults are watching TV, listening to the radio, reading, or taking a nap. Approximately 50% of older adults that use alcohol for sleep do not discuss their sleep difficulties with their healthcare provider.\textsuperscript{131} These self-treatments may worsen insomnia, and healthcare providers should routinely ask older patients about their sleep and the treatments that have been tried. This information will aid in the selection of the most appropriate therapy.

Over-the-counter (OTC) products are frequently chosen by older adults.\textsuperscript{131} These medications typically contain diphenhydramine or doxylamine, potentially inappropriate medications for use in the elderly patient. Due to the high potential of anticholinergic effects, possible mental status changes, and residual daytime drowsiness/excessive somnolence, OTC sleep products should be avoided in the elderly.\textsuperscript{123,134}

The use of other sedating antidepressants (e.g., trazodone and mirtazapine) for the treatment of insomnia should be reserved for elderly patients who have depression. Trazodone was commonly recommended by many experts as a safe medication for sleep before the availability of the benzodiazepine-receptor agonists;
however, there are no data to support this assertion. Antipsychotics with sedating adverse effects should be reserved for elderly patients with psychotic symptoms because of the multitude of adverse effects associated with their use.123,130,134,165

### Substance Use Disorders

*Etiology, Epidemiology, and Clinical Presentation Specific to Geriatrics*

Substance-use disorder is one of the leading causes of disability. With the elderly population increasing, and with the “Baby Boomers” now in their sixties, it appears the prevalence of late-life substance-use disorders will continue to increase.166-169 Alcohol abuse is noted to be a significant health issue for the elderly population, and over the last two decades more data have become available addressing the epidemiology, assessment, and treatment of late-life alcoholism.

Non-alcohol substance disorders include illicit and prescription drug abuse. Clinicians are more likely to encounter prescription abuse than illicit drug use in older adults.167,170 Currently, the prevalence of illicit drug use is very low in the elderly, even though it will likely increase as the geriatric population continues to grow.166-169 Due to the higher prevalence and moderate amount of data available, late-life alcohol and prescription drug use disorders will be the primary focus of this section.170

Recent reports note the majority of older adults (50% to 60%) are reported to abstain (no alcohol within the previous year) from alcohol compared to 30% to 40% of younger adults.171,172 The prevalence of alcohol-use disorder within community dwelling elderly is reported to be low (1% to 3%),172 but prevalence of unhealthy or at-risk drinking is higher (13% to 19%).170 In nursing homes, 29% to 49% of patients met criteria for alcohol-use disorder during their lifetime, with 10% to 18% having met criteria within 1 year of admission to the home.173,174

Two-thirds of older alcoholics developed alcoholism earlier in life and continued to drink through their elder years. These individuals are considered to have early-onset alcoholism. Late-onset alcoholism/abuse, which encompass the remaining one-third of older alcoholics, includes individuals who did not drink heavily until late in life. There are many differences between these groups regarding epidemiology and social history.175

Early-onset alcoholics are more likely to have a family history of alcoholism, socioeconomic decline due to their alcohol use, and antisocial behavior. Due to their many years of use, these patients will often have significant medical history such as cirrhosis, cognitive decline, and other psychiatric disorders. Late-onset alcoholics usually do not report any alcohol-related problems until after age 50. These individuals are often well educated and have maintained a high socioeconomic status through their working life. Alcohol-related illnesses are less frequent in this population. A stressful life event is usually what precipitates the excessive drinking. Late-onset alcoholics are noted to be more agreeable to treatment and recover more easily compared to early-onset patients.175,176 However, late-onset abuse and dependence are often missed by healthcare providers.170

Alcohol and drug abuse are often associated with other psychiatric illnesses in younger adults. Approximately 20% of older adults with a diagnosis of depression meet diagnostic criteria for alcohol-use disorder, and more than 90% of those who abuse alcohol have a history of depression.177 It has also been found that the prevalence of dementia is five times higher in elderly who are heavy drinkers compared to those who do not abuse alcohol.178

### Risk Factors for Alcohol Abuse and Comorbidities

Major risk factors include male gender, major life changes or stressors, and recent loss. Overall,
elderly women were found to be less likely to drink heavily; however, they are more likely than men to develop late-onset alcohol abuse.175

Although light to moderate consumption of alcohol has been shown to decrease risk of cardiovascular disease, diabetes, and dementia, heavy alcohol use is associated with increased morbidity and mortality.179-182 Morbidities associated with chronic alcohol use include pancreatitis, peptic ulcer disease, cirrhosis, thrombocytopenia, cardiomyopathy, hypertension, respiratory illnesses, and increased trauma from falls or motor vehicle accidents.171,183 Chronic alcohol use results in cognitive impairment, with cerebral atrophy and cerebellar degeneration. Cerebrovascular accidents are more common in alcoholics, which also result in significant cognitive and functional decline.175 Sleep disturbances are frequently reported by individuals who drink heavily, including those who use alcohol to help initiate sleep. Alcohol has been proven to decrease sleep maintenance, REM sleep, and delta sleep. For elderly alcoholics, the negative effects of alcohol on sleep are in addition to the reduced REM and deep sleep that accompany normal aging.184

Alcoholics are often deficient in several essential vitamins because of altered absorption and decreased intake. Vitamin B12 and folate deficiencies are common and can lead to macrocytic and hemolytic anemias, peripheral neuropathy, paresthesias, and weakness in the lower extremities if not supplemented.176 Thiamine deficiency results in both Wernicke encephalopathy and Korsakoff syndrome. Wernicke encephalopathy presents as acute confusion, ataxia, and abnormal eye movements, and Korsakoff syndrome presents as memory impairment.175

**Diagnostic Criteria**

According to the DSM-5, one meets criteria for a substance-use disorder if the use of a substance leads to significant impairment defined by two or more of the following and occurs within a 12-month period: (1) the substance is used in larger amounts or for a longer period of time than was intended; (2) there are continued efforts or unsuccessful attempts to decrease use; (3) a significant amount of time is spent seeking, using, and recovering from the substance; (4) one craves the substance; (5) recurrent use results in inability to meet obligations at work, home, or school; (6) abuse continues despite experiencing social and personal problems as a result; (7) normal social and work-related activities decrease because of substance use; (8) abuse occurs in situations that are dangerous (e.g., driving while intoxicated); (9) substance use continues despite the patient knowing concurrent illnesses and psychiatric disorders are related to the use; (10) tolerance develops; and (11) withdrawal symptoms occur when not using the substance.21

**Presentation Specific to Geriatric Patients**

Due to age-related physical changes, older adults have an increased sensitivity to alcohol and other mood-altering medications. As people age, lean body mass and total body water decreases, which leads to decreased distribution and higher serum concentrations of these substances.171 Impaired hepatic blood flow and reduced aldehyde-dehydrogenase can lead to reduced metabolism of alcohol.185 It and other abused substances can easily penetrate the CNS, making older adults more sensitive to the effects of these substances compared to younger adults. The interaction between alcohol and prescription medications, especially psychotropic medications, is a major concern in this age group.175

Because of these age-related factors, the recommended appropriate intake of alcohol for older adults is lower than the standards established for young to middle-age adults. The National Institute on Alcohol Abuse and Alcoholism186 and the Substance Abuse and Mental Health Services Administration Treatment Improvement Protocol170 recommend no more than one standard drink per day and no more than two standard drinks on any occasion for adults older than 65. A standard drink is defined as 5 ounces of wine, 12 ounces of beer, or a
mixed drink containing 1.5 ounces of hard liquor. Use beyond these recommendations is considered hazardous or at-risk drinking.\\textsuperscript{167}

Many geriatric and substance-abuse specialists agree there are limitations with using the DSM-5 criteria to diagnose substance-use disorders in the elderly.\\textsuperscript{167} Because of these limitations, it is suspected there is low reporting in older adults. As mentioned, one of the criteria for substance-use disorder is developing tolerance, which is usually shown by increased use of the substance to obtain the same level of effect. For older adults, substance use may appear to decrease or stay the same due to increased sensitivity and higher blood levels at lower amounts. Lower quantities used may also make it difficult for older users to meet the criterion of spending a great deal of time in activities related to substance use.\\textsuperscript{187} The criterion of withdrawal may not be applicable for patients who develop late-onset substance dependence and have not yet experienced a period of withdrawal.\\textsuperscript{175} Finally, because older adults are often retired or isolated from social situations, compared to younger adults, the criterion of failing to meet daily obligations because of substance use is not as likely to apply to many late-life substance users.\\textsuperscript{167}

### KEY POINT

Limitations exist when using the DSM-5 criteria for substance-use disorders to diagnose geriatric patients. These limitations result in underdiagnosis of late-life substance abuse.

#### Screening for Alcohol Dependence or Hazardous Drinking

Alcohol abuse/dependence screening should be part of a patient’s regular physical examination and done at least yearly.\\textsuperscript{170} Common screening tools used in older adults include the Short Michigan Alcoholism Screening Test–Geriatric version (SMAST-G), the CAGE questionnaire, and the Alcohol Use Disorders Identification Test (AUDIT). Out of the three screening tools, the SMAST-G was developed specifically for older adults.\\textsuperscript{167} The CAGE questionnaire is considered the easiest to use in a clinic setting and has high specificity for detecting alcohol abuse. However, it has low sensitivity for detecting alcohol dependence and at-risk drinking.\\textsuperscript{171,175} Patient self-reporting continues to be the primary method of obtaining history of alcohol use, although any collateral information from the patient’s spouse and family is helpful.\\textsuperscript{171} If a patient states he or she abstains from alcohol, clinicians should continue to question the reasons for abstaining. Some individuals currently abstain from alcohol because of abuse problems in the past.\\textsuperscript{171}

### Common Problems Encountered When Treating Elderly Patients

#### Ethanol Withdrawal and Acute Treatment

Older age has not been shown to increase risk of drug and alcohol withdrawal. However, older adults may experience longer duration of withdrawal symptoms and are more likely to have complications due to a longer history of alcohol abuse, medical comorbidities, baseline cognitive impairment, and sensitivity to drug treatments.\\textsuperscript{171,188} Older age has also been associated with longer hospital stays for treatment and greater risk of being discharged to an extended-care facility.\\textsuperscript{189}

Patients experiencing alcohol withdrawal typically present with autonomic hyperactivity, including increased pulse and blood pressure, increased temperature, restlessness, anxiety, tremor, and insomnia. These symptoms usually present within the first 12–48 hours after the last drink consumed. Severe symptoms, such as hallucinations, delirium tremens, seizures, and coma, can develop as late as 2–10 days after withdrawal. Because alcohol withdrawal can be severe and fatal, careful evaluation and benzodiazepine regimens should be made available as recommended using the Clinical Institute Withdrawal Assessment (CIWA) tool (Table 13-3).\\textsuperscript{175,188,190}

Patients who are predicted to have minimal to moderate withdrawal symptoms, no history of
complicated withdrawal, no significant comorbidities, and who have a caregiver available to monitor closely may complete the detoxification process as an outpatient. The patient and caregiver should be educated on how to use the CIWA (Table 13-3) to assess the severity of withdrawal symptoms. If the patient experiences moderate withdrawal (CIWA score between 8 and 15), then a benzodiazepine can be administered to help relieve symptoms. The CIWA should be used every 4 hours, and a clinician should follow up with the patient daily during the withdrawal period.188

Patients should be admitted for inpatient detoxification if they have a history of withdrawal delirium or seizures, complex medical or psychiatric illnesses, suicidal thoughts, no strong support system, or a CIWA score >15. Hospitalization can also provide further benefits, such as lack of access to alcohol and a new environment.188

For relief and prevention of alcohol withdrawal symptoms, benzodiazepines are first-line therapy for all patients, including older adults. They act on the GABA A-type receptor, similar to alcohol, and augment the inhibition effect of GABA. Much data exist showing benzodiazepines reduce the risk of delirium and seizures during withdrawal.188 However, the choice of benzodiazepine (long-acting versus short-acting) to treat elderly patients is not as clear. As discussed, long-acting benzodiazepines with active metabolites may be less tolerated in the elderly due to age-related pharmacokinetic and pharmacodynamic changes. The adverse effects of these benzodiazepines may be one of the reasons more complications and longer hospital stays have been observed in

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**Table 13-3. Clinical Institute Withdrawal Assessment for Alcohol**

<table>
<thead>
<tr>
<th>Symptom</th>
<th>Range of Scores^a</th>
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| Agitation             | 0 = normal activity  
|                       | 7 = constantly moving |
| Anxiety               | 0 = calm, at ease  
|                       | 7 = acute panic symptoms |
| Auditory hallucinations | 0 = no hallucinations  
|                       | 7 = continuous hallucinations |
| Disorientation        | 0 = oriented, no cognitive impairment  
|                       | 4 = disoriented to time, place, and person |
| Headache              | 0 = no pain  
|                       | 7 = extremely severe |
| Nausea/vomiting       | 0 = no GI symptoms  
|                       | 7 = constant nausea/vomiting/dry heaves |
| Sweating              | 0 = no sweating  
|                       | 7 = drenching sweats |
| Tactile hallucinations | 0 = no hallucinations  
|                       | 7 = continuous hallucinations |
| Tremor                | 0 = no tremor present  
|                       | 7 = severe tremor |
| Visual hallucinations | 0 = no hallucinations  
|                       | 7 = continuous hallucinations |

^aMaximum score is 67. Minimal/mild withdrawal symptoms score <8, moderate withdrawal symptoms score 8–15, severe withdrawal symptoms score >15.
elderly patients undergoing detoxification versus younger adults.189,191,192

Based on the possible risk of adverse effects with long-acting benzodiazepines, clinicians may wish to use short-acting agents, such as lorazepam or oxazepam, for withdrawal treatment in the elderly. However, one should also keep in mind the risk: it is possible a patient may not be provided adequate coverage of withdrawal symptoms with short-acting agents.188 A recommended practice is to start with diazepam, using the CIWA protocol. The patient should be monitored closely for adverse effects of the medication. If they occur, then therapy can be switched to a shorter-acting benzodiazepine if withdrawal coverage is still needed.

Unless an older patient has a seizure disorder, history of alcohol withdrawal seizures, or history of delirium tremens scheduled benzodiazepine regimens are not recommended. For most cases of detoxification, a symptom-triggered approach, such as a CIWA protocol, should be used to prevent unneeded benzodiazepine use.188

In addition to treating withdrawal symptoms, electrolytes and vitamins should be supplemented, if needed. Thiamine supplementation (100 mg daily) should be provided in all cases of alcoholism. Vitamin B12 and folate are also recommended if serum levels are low or macrocytic anemia is present. Electrolytes, especially magnesium, should be checked and corrected if abnormal.175

**KEY POINT:** Although short-acting benzodiazepines are usually recommended over long-acting agents for elderly patients, short-term use of long-acting benzodiazepines is more likely to ensure adequate coverage during withdrawal without increasing risk of seizures. Careful dosing and diligent monitoring are required.

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**Long-Term Treatment for Alcohol Dependence**

Treatment research for late-life substance-use disorders is lacking, but published data have slowly emerged over the last two decades, especially for alcohol treatment. Studies have shown psychosocial and pharmacological treatments to be effective for older adults and result in increased quality of life.171 Community programs for elders assisting with alcohol abstinence have shown to be just as or more beneficial in improving quality of life compared to middle-aged adults.192-194

Brief advice during clinic visits has been shown to significantly decrease drinking in the elderly. Several studies have demonstrated that 10–15 minutes of counseling regarding alcohol use can significantly reduce drinking compared to usual-care patients.194-196 In addition, two large trials were performed to investigate the effectiveness and feasibility of implementing brief advice in primary care and within community screening programs.197,198 Psychosocial intervention is considered the cornerstone of therapy when treating substance-use disorders and maintaining sobriety. It has also been beneficial for older adults and, interestingly, the best results are observed when older patients are involved in age-specific programs versus mixed-age groups. Studies have shown older adults to have higher program completion rates, higher group attendance, and higher abstinence rates at 6 months and 1 year after completing a program when placed in age-specific versus mixed-age programs.199-201 They should include the following: (1) group therapy with other older adults that is supportive and helps build self-esteem; (2) a focus on coping with common psychosocial issues in the elderly such as depression, loneliness, and loss of spouse; (3) a focus on increasing social support for the patient; (4) clinicians who are experienced in working with the elderly; and (5) an ability to refer patients to a case manager and other outside services.169,187
KEY POINT: Psychosocial intervention is considered the cornerstone of therapy when treating substance-use disorders and maintaining sobriety. Age-specific programs have been shown to work best for older adults.

Three agents (disulfiram, naltrexone, and acamprosate) are currently FDA approved to help maintain abstinence from alcohol. All have been shown to be most efficacious when used along with psychosocial therapy. Patients should understand that pharmacotherapy is prescribed as an adjunct and not as a replacement for individual or group therapy.

Disulfiram is the oldest agent available for treatment of alcohol dependence. It is used as a deterrent from drinking in order to avoid the symptoms associated with the alcohol-disulfiram interaction and is not recommended for elderly patients because of the adverse effects of acetaldehyde and the risk of exacerbating concurrent illnesses.

Naltrexone is an opioid antagonist with a recommended dosing of 50 mg daily orally or 380 mg monthly if given intramuscularly. The most common adverse effects reported are GI symptoms (nausea, stomach pain, anorexia) and injection site reactions with the parenteral product. Elevation in liver transaminases and hepatotoxicity are reported for both the oral and injectable drug. Therefore, baseline liver function tests should be obtained and monitored periodically with therapy. Naltrexone should not be used in patients with history of liver impairment or those taking opioid therapy.

Acamprosate is the newest agent approved for maintenance of alcohol abstinence. It is recommended that acamprosate be initiated after detoxification and sobriety of at least 7 days. A dose of 666 mg three times a day is normally prescribed. Although food has no significant effect on absorption of acamprosate, patients may be encouraged to take it with meals to increase compliance. The medication is renally cleared; therefore, dose adjustments should be made for decreased renal function. Patients with a creatinine clearance between 30 and 50 mL/min should start with 333 mg three times daily, and it should not be used in patients with creatinine clearance of <30 mL/min. Acamprosate is usually well tolerated, and diarrhea is the most common adverse effect. To date, there have been no trials published addressing the efficacy of acamprosate in the elderly. It is suspected the medication should be well tolerated in older adults without exacerbating any chronic diseases. However, many elderly should be dosed the lower dose (333 mg three times daily) because of age-related renal impairment.

Nonmedical Prescription Drug Use

The prevalence of nonmedical prescription drug use is noted to range from 0.14% to 1.4% in patients age 50 and older. Prescription drug abuse appears to be uncommon among elderly, especially if they do not have a history of other types of substance abuse. Risk factors include female gender, depression, social isolation, and history of alcohol and other substance abuse. Late-life abusers usually do not have to use illegal methods to obtain controlled substances. Unsafe amounts of medications are often obtained by using multiple physicians, borrowing medication from family and friends, or by keeping and collecting prescriptions over time.
Benzodiazepines may be of concern for abuse due to their addiction potential, and they continue to be one of the most prescribed medications in the elderly. Benzodiazepines are used for many psychiatric symptoms, such as agitation, anxiety, and insomnia. As discussed, chronic use should be avoided in the elderly if possible because of the high risk of adverse effects in this population. If the use of benzodiazepines outweighs the risks, then shorter-acting agents such as lorazepam and oxazepam are recommended, and use should be limited to no more than 4 months. For patients who are at risk for abuse, highly lipophilic agents such as diazepam and alprazolam should be avoided.

Benzodiazepine withdrawal symptoms are more likely to present as confusion and disorientation in older adults rather than increased anxiety and insomnia, often witnessed in younger adults. Treatment of benzodiazepine abuse is gradual tapering of the medication. Patients addicted to short-acting benzodiazepines such as alprazolam should be switched to a longer-acting agent first (clonazepam is a popular choice). The longer-acting benzodiazepine can then be slowly tapered. Benzodiazepine withdrawal symptoms are more likely to present as confusion and disorientation in older adults rather than increased anxiety and insomnia, often witnessed in younger adults. Treatment of benzodiazepine abuse is gradual tapering of the medication. Patients addicted to short-acting benzodiazepines such as alprazolam should be switched to a longer-acting agent first (clonazepam is a popular choice). The longer-acting benzodiazepine can then be slowly tapered.

Opioid prescribing has increased significantly over the last 15 years for all age groups to meet national standards for adequate pain control. Since the start of the “right to pain relief” movement in the late 1990s, it has increased by 149%. Consequently, both rates of opioid abuse and overdose have increased as well. In the elderly population, recent studies have also shown an increased risk of falls, fractures, and myocardial infarctions with the chronic use of opioids. To provide adequate pain control for patients but minimize the risks associated with opioid overprescribing, national programs and policies have recently been implemented. The FDA now requires a Risk Evaluation and Mitigation Strategy (REMS) from manufacturers of long-acting opioid products. Requirements of the REMS may include specialty certification from prescribers and registry of patients for national monitoring. In addition to the REMS program, several state medical boards have adopted the Federation of State Medical Boards Model Policy for the Use of Controlled Substances for the Treatment of Pain. Physicians in these states are required to provide a thorough evaluation of patients who complain of pain, which includes assessing substance abuse history. A detailed treatment plan is developed, documented, and signed by the physician and patient. These documents along with the records of ongoing care of the patient are saved and archived.

Clinicians should be aware that drug-seeking behavior can also be the result of inadequate pain control. Chronic opioid users will develop physical dependence and can experience uncomfortable withdrawal symptoms such as hyperalgesia, diarrhea, nausea, rhinorrhea, shivering, anxiety, and agitation if therapy is discontinued abruptly. Physical dependence can occur, even if addiction is not present. Whether abuse is suspected or the patient simply wishes to discontinue therapy, opioids should be gradually tapered to prevent withdrawal. This is true for opioids of lower abuse potential also, such as tramadol. Tapering the daily dose by 10% per week is recommended. A more rapid taper of 25% to 50% every few days is appropriate for those abusing opioids.
**Case 1: Major Depressive Disorder, Moderate to Severe**

**Subjective:**

TM is a 72-year-old male patient who presents to his primary care provider for the first time in 5 years with complaints of stomach and joint pain, trouble sleeping, increased anxiety, impaired concentration and short-term memory, and lack of energy. TM is worried he has something seriously wrong with him such as cancer.

After interviewing the patient, it is also discovered TM is no longer exercising or visiting the community senior center as he did in the past. He mentions that he is getting old and his joint pain has worsened over the last year to a point where he has trouble walking. TM states, “I’m not sure why I’m still alive. I wish I would just pass in my sleep.” TM becomes tearful when he talks about his deceased wife.

**Medications:**

No prescription medications, has been using OTC omeprazole 20 mg daily for stomach pain and uses occasional acetaminophen for joint pain.

**Past Medical History:**

Obstructive sleep apnea (uses CPAP as prescribed), osteoarthritis.

**Allergies:**

NKDA.

**Family History:**

Both parents are dead, but neither parent had a history of mental illness.

**Social History:**

TM’s wife died unexpectedly a year ago while hospitalized for pneumonia. He has three children and six grandchildren, but they all live out of state. He denies alcohol, tobacco, or illicit drug use.

**Objective:**

Ht 70˝, Wt 265 lb, BP 138/89 mmHg, P 65 BPM, pain = 7/10.

**Labs:**

Basic metabolic panel and complete blood count are normal, TSH 3.5 milli-International Units/L; vitamin B12 450 mg/mL.

**Assessment:**

TM meets the diagnostic criteria for major depressive disorder, moderate to severe. He has decreased interest in his daily activities, trouble sleeping, decreased energy, memory complaints, and passive suicidal ideation. In addition, he has symptoms of generalized anxiety, with trouble sleeping, decreased energy, impaired concentration, and anxiety. He also complains of joint and stomach pain, which may be associated with his depression.

**Plan:**

1. Sertraline 25 mg can be offered to the patient as a first-line agent. Begin 25 mg daily ×1 week then titrate to 50 mg daily.
2. Refer patient to the neuropsychologist for psychotherapy, if patient agrees.
3. Begin scheduled acetaminophen 1,000 mg every 8 hours for joint pain.
4. Return to clinic in 1 week.
**Rationale:**

1. Psychotherapy and medication therapy should be offered to the patient for optimal treatment. Sertraline, citalopram, or escitalopram are appropriate choices for a first-line SSRI as they have a favorable pharmacokinetic profile for older adults and are available as generic medications.

2. Because TM has several risk factors for suicide (age, white male, chronic pain, immobility, isolation), he should be followed frequently in the beginning of therapy (every week or every other week). Further work-up for stomach and joint complaints may be required, but symptoms may improve as depression is treated. This can be addressed at his return appointment.

**Case Summary:**

TM is a 72-year-old man who suffered the loss of his wife 1 year ago and now presents with late-onset depression and anxiety. He also has somatic complaints of stomach and joint pains. Some thoughts of death are evident, which increase concern that he may consider suicide. He is not on medications associated with depression. The stomach and joint pain may be separate diagnoses or may be associated with his depression. Treatment with an SSRI is appropriate to begin, as is more effective management of his pain symptoms with acetaminophen.
Case 2: Insomnia

Subjective:
SB is an 81-year-old male who presents to his primary care physician for routine physical exam. On questioning, SB states that he is concerned he is not getting a full 8 hours of sleep at night. He complains of having difficulties falling asleep and waking up several times during the night, sometimes with shortness of breath. He denies fevers, chills, nocturia, dysuria, or dyspnea. SB wakes up well-rested and is able to perform his usual activities of daily living and instrumental activities of daily living without drowsiness.

Social History:
Negative for tobacco use, occasional alcohol use during special occasions. SB recently started drinking 1–2 beers to help him feel sleepy before bedtime.

Objective:
PMH: BPH, HTN, CHF; BP 152/78, P 76 BPM (sitting), BP 148/78 P 78 BPM (standing).

Medications:
Terazosin 1 mg at bedtime, finasteride 5 mg daily, furosemide 20 mg twice daily, lisinopril 20 mg every morning, aspirin 81 mg daily. OTC/herbals: none.

Physical Examination:
Within normal limits except trace pitting edema in ankles bilaterally and a slightly enlarged prostate.

Labs:
Urinalysis negative.

Assessment:
SB is an 81-year-old man who presents with concerns about his total sleep time, sleep latency, and frequent nocturnal awakenings. He has several modifiable factors that can exacerbate insomnia to be addressed before hypnotic therapy is considered. He may be experiencing adverse outcomes associated with his current drug regimen that are exacerbating insomnia, either via adverse effects or poor disease state control.

Plan:
1. Educate patient on the normal changes in the elderly that may be affecting his sleep pattern and in daily routines that affect sleep hygiene. Educate patient on proper sleep hygiene and offer cognitive behavioral therapy.
2. Discontinue alcohol consumption before bedtime. Caution patient on self-treating with OTC sleep aids. These interventions may worsen his sleep complaints and his comorbid conditions.
3. Recommend reevaluation of his heart failure regimen with other members of the care team. Specifically, evaluate the administration times of furosemide and consider adjustment of the dose to avoid a diuretic effect at night. Evaluate whether optimizing his heart failure regimen may improve heart failure symptoms in general, and sleep symptoms specifically.

Rationale:
Because SB wakes up well-rested without daytime drowsiness, pharmacologic treatment with a hypnotic medication is not necessary at this time. However, interventions can be made to reduce the contribution that alcohol or evening doses of furosemide may contribute to poor sleep patterns. In addition, education about daily routines and sleep hygiene can assist with
the promotion of healthy sleep patterns. At this visit, there are not enough data to critically and completely evaluate his heart failure therapy, but SB’s current symptoms warrant a review of disease state control and drug therapy.

**Case Summary:**

SB’s case illustrates examples of both nonpharmacological and nonhypnotic pharmacological approaches that can be considered for a patient presenting with complaints about insomnia. The addition of a hypnotic at this time might provide some immediate relief, but it is possible that any benefit would be limited if underlying problems are not corrected. Due to the chronic nature of the comorbidities in this case, the use of hypnotic medication to mask ongoing symptoms has the potential to become a nightly, long-term routine.
# Chapter Summary

Depression and GAD are the most common psychiatric disorders observed in geriatric patients and if left untreated lead to decreased daily function and increased morbidity and mortality. SSRI and SNRI therapy are recommended as first-line when medications are needed. Doses should be started at the lower end of the range but eventually titrated to a moderate dose to provide an adequate response. Frequent follow-up, monitoring, and support should be provided once therapy is initiated to increase chances of remission, compliance, and quality of life.

Benzodiazepines can be used if acute treatment of an anxiety disorder is needed. Short-acting agents such as lorazepam and oxazepam are the preferred agents to use in the elderly. Generally, chronic benzodiazepine use is discouraged because of the risk of adverse effects and should be gradually tapered after a patient has had time to respond to antidepressant therapy.

Insomnia is a common complaint among elderly patients. If left undiagnosed and untreated, insomnia may adversely affect a patient’s overall health status and quality of life. When an older patient complains of sleep difficulties, it is important to evaluate the patient as a whole, which includes assessing comorbid conditions, medication use, and environment. Assessing the elderly patient’s daytime functioning can help the clinician in selecting the appropriate therapy. Nonpharmacologic therapy is beneficial for the elderly. If nonpharmacologic strategies are ineffective, the use of drug therapy (e.g., a benzodiazepine-receptor agonist, ramelteon, or doxepin) may be warranted.

The prevalence of substance-use disorders in older adults is less than that observed in young to middle-age adults. However, as the geriatric population continues to grow and the “Baby Boomers” begin to enter their sixties, the prevalence of late-life abuse is expected to increase. Currently, alcohol abuse is noted to be more concerning in the elderly population compared to prescription drug or illicit substance abuse.

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**Clinical Pearls**

- Older adults with sleep difficulties often try self-treatment interventions before reporting these symptoms to their healthcare provider. Interventions often tried are watching TV, listening to the radio, OTC sleep aids, or drinking alcohol, which may worsen insomnia or cause adverse effects. When assessing older adults, ask about their sleep and sleep habits, including any treatments that they have tried to help them sleep.

- Current federal regulations require periodic dose reductions for all psychoactive medications for nursing home residents. Antidepressants, benzodiazepines, and benzodiazepine-receptor agonists must be tapered to lower doses within 6 months to meet this regulation. This is repeated until the medication is discontinued or until the resident demonstrates symptoms of disease recurrence. This is problematic with the use of antidepressants, which are recommended for use a minimum of 9 months with late-life depression and sometimes needed for life-long therapy. Clear documentation of need is necessary to ensure optimal pharmaceutical care and prevent placing the nursing home at risk for regulatory noncompliance.
**Self-Assessment Questions**

1. What other complaints are associated more with late-life depression and late-life anxiety compared to young adult depression and anxiety?

2. Which therapies are considered first line for treatment of late-life depression and late-life anxiety?

3. Which benzodiazepines are considered safer for older adults? When and how should benzodiazepines be discontinued?

4. What physiologic changes on sleep architecture, circadian rhythm, and homeostatic drive occur as a patient gets older? How do chronic diseases and medication use contribute to sleep disturbances in elderly patients?

5. Of the available pharmacologic therapies indicated for insomnia, which are preferred in the elderly population and why?

6. What are the limitations of using the DSM-5 criteria to diagnose a geriatric patient with substance abuse and dependence?

7. Which pharmacologic agents can be considered as adjunct therapy for older adults trying to abstain from alcohol?

8. Which classes of prescription medications are more likely to be abused because of increased prescribing in the elderly population?

**References**


161. Mets MA, de Vries JM, de Seonerpont Domis LM, et al. Next-day effects of ramelteon (8 mg), zopiclone (7.5 mg), and placebo on highway driving performances, memory functioning, psychomotor performance, and mood in healthy adult subjects. *Sleep*. 2011;34:1327–1334.


Learning Objectives

1. Discuss the risk factors and etiology of cataract, glaucoma, macular degeneration, and dry eye.
2. Evaluate the evidence supporting treatment guidelines for vision disorders and pain in elderly patients.
3. Recommend a therapeutic regimen for vision impairment based on appropriateness, efficacy, and adverse effects.
4. Discuss how physical impairments, cost, and complex regimens may impact medication adherence in elderly patients with glaucoma.
5. Describe strategies for improving communication with patients with vision and hearing impairment.
6. Describe the etiologies and presentation of persistent pain in elderly patients.
7. Explain the challenges in assessing and treating pain in elderly patients with or without cognitive impairment.
8. List the classes of medications commonly used to treat nociceptive and neuropathic pain.
9. Discuss common adverse effects of medications that impact treatment decisions in elderly patients with pain.

Key Terms and Definitions

Breakthrough Pain: Acute pain that occurs despite consistent treatment with long-acting analgesia.

Dermatome: Localized region of skin that is innervated by a single nerve root.

Drusen: Yellow or white deposits on the retina that are more common in older patients; correlated with the risk of developing macular degeneration.
**MACULAR DEGENERATION:** Eye disease of the macular retina affecting central vision; classified as either exudative/neovascular or nonexudative.

**NEUROPATHIC PAIN:** Pain initiated or caused by a primary lesion or dysfunction in the nervous system.

**NOCICEPTORS:** Receptors preferentially sensitive to a noxious stimulus or to a stimulus that would become noxious if prolonged.

**PRESBYCUSIS:** Bilateral, high-frequency hearing loss that is the most common hearing disorder in older patients.

**PRESBYOPIA:** Inability to focus near vision due to decreased lens accommodation.

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**Introduction**

Sensory deficits in the elderly are a chief contributor to decreased quality of life. As vision, taste, smell, and hearing diminish, simple daily pleasures are reduced. Loss of vision or hearing is especially difficult and contributes to increased dependence on others for activities of daily living. In addition, the sense of touch may become altered with neuropathy from a variety of etiologic sources. Pain management is especially problematic in older adults because of the effects of analgesic medications on the senses and the major organ systems. This chapter focuses on vision and hearing loss, pain management, and the pharmacotherapy associated with these disorders.

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**Vision and Hearing Impairment**

**Etiology, Epidemiology, and Clinical Presentation Specific to Geriatrics**

Visual impairment in geriatric patients is largely due to age-related changes in the eye that may be either structural or functional in nature (Table 14-1). Presbyopia, a functional change, and increased intraocular pressure, a structural change, are common with aging. Increased intraocular pressure is a risk factor for glaucoma. Another functional change, reduced tear production, results in dry eyes, but there may also be an inflammatory component. Other etiologies of visual impairment include cataract, macular degeneration, and diabetic retinopathy.

Visual impairment affects an estimated 3.3 million people in the United States over the age of 40 and is projected to increase to 5.5 million (3.6% of the population) in the year 2020. Race, ethnic group, and age account for differences in prevalence of low vision and blindness. Cataract is the most common cause of low vision across ethnic groups, and in African Americans, cataract is also the leading cause of blindness. Macular degeneration and glaucoma are the leading causes of blindness in white and Hispanic persons, respectively. Depending on ethnic group, blindness and low vision is estimated to increase two- to eightfold after age 80.

The etiology of hearing loss falls into two categories, conductive and sensorineural. Kerumen impaction, excessive noise, cerebrovascular accident, trauma, tumors, ototoxic medications, and presbycusis are common causes. The prevalence of hearing loss increases with age. Close to 17% of adults in the United States report hearing loss. This number increases to 47% in people ages 75 and above. Hearing loss is common and may go undetected because of its gradual onset or apprehension on the part of the patient when admitting impairment.

Elderly patients may experience visual and hearing impairments because of natural age-related declines, but drug-induced causes may be present, either due to chronic toxicities or increased sensitivity to adverse effects. For
instance, antipsychotic medications have been associated with cataracts, as has corticosteroid use in the context of both cataracts and open-angle glaucoma, whereas anticholinergics and adrenergics have both been associated with acute closed-angle glaucoma. Antimicrobial antibiotics and nonsteroidal anti-inflammatory drugs (NSAIDs) are common contributors to ototoxicity.

Comorbidities also increase risk for visual issues in older patients. Sjögren’s syndrome, an autoimmune disease that affects exocrine glands, increases the risk for dry eye. Diabetes is the most common cause of retinopathy and a possible risk factor for cataract and glaucoma.

Functional losses and emotional problems are consequences of visual and hearing impairment. Both activities of daily living and self-administration of medication can become limited. Depression, social isolation, and cognitive impairment are reported consequences of declining hearing and vision.

### Table 14-1. Age-Related Eye Changes

<table>
<thead>
<tr>
<th>Functional</th>
<th>Presbyopia</th>
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<tbody>
<tr>
<td></td>
<td>Decreased refractive power</td>
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<tr>
<td></td>
<td>Decreased dark adaptation</td>
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<tr>
<td></td>
<td>Decreased contrast sensitivity</td>
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<tr>
<td></td>
<td>Visual field constriction</td>
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<tr>
<td></td>
<td>Decreased tear production, resulting in dry eyes</td>
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<tr>
<td></td>
<td>Increased difficulty with upward gaze, convergence</td>
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<tr>
<td>Structural</td>
<td>Lens enlargement, resulting in narrowing of the anterior chamber angle</td>
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<tr>
<td></td>
<td>Decreased lens translucency, resulting in decreased retinal illumination</td>
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<tr>
<td></td>
<td>Increased lens stiffness and decreased curvature</td>
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<tr>
<td></td>
<td>Rod cell loss</td>
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<tr>
<td></td>
<td>Liquefaction of vitreous gel</td>
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<tr>
<td></td>
<td>Loss of eyelid tone, resulting in entropion or ectropion</td>
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<tr>
<td></td>
<td>Rising intraocular pressure</td>
</tr>
</tbody>
</table>

Source: Adapted with permission from Lewis T, Warshaw G. Current Geriatric Diagnosis and Treatment. ©2004. McGraw-Hill Education, LLC.

**Summary of Standard Treatment in General Adult Population**

Management of glaucoma is targeted at decreasing intraocular pressure and preventing angle closure. First-line pharmacotherapy for primary open-angle glaucoma includes topical beta blockers or prostaglandin analog eye drops. Prostaglandin analogs appear to be the most effective initial option but may be more expensive. Other pharmacotherapeutic options include topical alpha-2 adrenergic agonists, topical or oral carbonic anhydrase inhibitors, and topical parasympathomimetic agents.

Decreasing intraocular pressure in primary open-angle glaucoma is accomplished by either decreasing aqueous production or increasing its outflow. Beta-adrenergic blockers and carbonic anhydrase inhibitors decrease aqueous humor production (Table 14-2). Prostaglandin analogs and cholinergic agents increase outflow of aqueous humor. Alpha-adrenergic agonists perform both of these actions. A 20% reduction of intraocular pressure is often the initial goal of pharmacotherapy. It is recommended that if one agent is effective but a target intraocular pressure has not been reached, then combination therapy should be used. However, if one agent is ineffective, an alternative drug class should be used.
Nonpharmacologic approaches to mild dry eye, such as minimization of medications and modification of environmental factors that may worsen dry eye, are recommended. The common management of dry eyes includes lubricant and anti-inflammatory eye drops. Lubricant eye drops, gels, or ointments are effective in both mild and severe disease. Preservative-free tear substitutes are recommended when they are used frequently. The efficacy of lubricants is limited by short contact time with the eye. Hypotonic solutions, tear stabilizing molecules, and lipid formulations have enhanced contact time with the eye and the viscosity and stability of the tear film.

Cyclosporine and corticosteroid eye drops inhibit inflammation and increase the health of the ocular surface. With both of these agents, little systemic absorption occurs, although prolonged use of topical corticosteroids is not recommended because of minimal efficacy in clinical trials and increased risk of cataract development and elevated intraocular pressure. Other methods to treat dry eyes have been examined in smaller trials and demonstrate modest benefit.
Oral omega-3 fatty acid supplementation has resulted in minimal improvement in dry eye in clinical trials and may be used. Topical or oral secretagogues and hormone replacement have been studied or used off-label for dry eye. New agents that blunt inflammatory responses in the eye (e.g., interleukin-1 and T-helper cells) are currently being studied in clinical trials and represent new pharmacologic targets in the treatment of dry eye disease.

The treatment for cataract is primarily surgical. Although many studies have examined nutritional supplementation, such as beta-carotene, to reduce the incidence of cataract, they have been largely unsuccessful. Recommended methods to prevent cataract are aimed at nonpharmacologic methods, such as smoking cessation, avoidance of certain medications that may cause cataract, and reduction of sun exposure.

For age-related macular degeneration (AMD), no pharmacologic prevention is recommended, and treatment depends on the type of AMD, either wet or dry. Initial treatment of dry, or atrophic, AMD is reserved until there is intermediate macular degeneration, evidenced by the presence of drusen in both eyes, or advanced disease in one eye, evidenced by drusen and blurred vision. Oral antioxidant vitamin and mineral supplements that include vitamin C, vitamin E, beta-carotene, copper, and zinc are the treatments of choice in mild disease or advanced dry AMD, as determined by a group of studies undertaken by the Age-Related Eye Disease Research Group. As beta-carotene has been associated with increased risk for lung cancer, a smoker’s formulation is available without this vitamin.

**KEY POINT:** Use of eye formulations consisting of antioxidants and minerals for prevention of cataract or AMD is not currently recommended.

When evidence of neovascularization is present in a patient with AMD, referred to as wet AMD, treatment with periodic intravitreal injections of anti-vascular endothelial growth factor (anti-VEGF) agents ranibizumab, bevacizumab, and pegaptanib is currently recommended. Ranibizumab and bevacizumab are the most recently studied anti-VEGF agents that reduce angiogenesis in macular degeneration, although bevacizumab is an older agent that is used off-label for AMD. They are typically dosed monthly, but guidelines allow for clinical judgment regarding follow-up treatment, which may result in less frequent administration. In more advanced neovascular disease, photodynamic therapy with verteporfin, an agent that destroys abnormal blood vessels, may be used. Further study on newer anti-VEGF therapies such as aflibercept, combination therapy with different anti-VEGF agents, or anti-VEGF agents with photodynamic therapy may reveal new treatment directions.

Treatment of hearing loss depends on the etiology. Hearing may be restored if the causes are treatable, such as cerumen impaction, seasonal allergies, or a brain tumor. However, in cases where the cause is irreversible, management of the hearing loss with hearing aids, assistive listening devices, or cochlear implants may be necessary. The decision as to what kind of aid is most beneficial is the specialty practice of audiologists.

**Review of Evidence Supporting Treatment Recommendations for Elderly Patients**

The presence of visual impairment increases with age, emphasizing the importance of follow-up eye examinations, even in the oldest patients. Most studies do not specifically evaluate the results of elderly patients who are enrolled, but the majority of subjects are typically over the age of 65, except in glaucoma studies, where the average age tends to be younger.

Monotherapy with prostaglandin analogs or beta-adrenergic blockers is recommended in glaucoma guidelines. Bimatoprost, a prostaglandin analog, was compared to twice-daily
timolol in patients with an average age of 60, ranging up to 90. Once-daily bimatoprost significantly reduced intraocular pressure compared with timolol. Twice-daily dosing of bimatoprost was not more beneficial than once-daily dosing. Once-daily latanoprost lowered intraocular pressure more than twice-daily timolol in chronic, closed-angle glaucoma. The average age of participants was 63. Aside from ocular hypertensive effects, latanoprost showed a significant improvement in contrast sensitivity compared with timolol in a study of patients with an average age of 61, ranging up to 69. A preservative-free formulation of a prostaglandin analog, tafluprost, was compared with twice-daily timolol in a 12-week study. The mean age of subjects was 63. The intraocular pressure lowering of tafluprost was noninferior to timolol, but its primary role is to serve as an alternative treatment for patients with allergies to preservative-containing formulations.

Combination therapy is commonly studied because of the additive effects of two classes of medications versus monotherapy. A combination of brimonidine, an alpha-adrenergic agonist, and timolol demonstrated significantly greater reductions in intraocular pressure compared with either agent alone. A study of over 200 patients randomized to either a timolol plus latanoprost group or timolol plus dorzolamide, a carbonic anhydrase inhibitor, demonstrated that the combination with latanoprost significantly lowered intraocular pressure more than the dorzolamide combination. A fixed-dose combination product with brimonidine and brinzolamide, a carbonic anhydrase inhibitor, demonstrated significantly more intraocular pressure lowering when compared with each agent as monotherapy. The mean age of patients was 64, but about 50% of patients were over 65. Using multiple single-agent formulations or fixed-dose combination products may be an option in elderly patients who do not achieve adequate results with monotherapy.

Trials in the management of dry eye disease are not specific for older patients. One study of topical cyclosporine demonstrated significant symptomatic improvement of mild-to-moderate dry eye and objective improvement in severe dry eye. These patients ranged in age from 23 to 88, with an average age of 63. Blurred vision, grittiness, itchiness, and dryness were significantly decreased from baseline in cyclosporine treatment groups compared to a placebo vehicle in another study, where the mean age of participants was 60. Objective measures were also significantly improved. Consumption of omega-3 fatty acids may improve dry eye. In studies ranging from 30 days to 3 months, the use of omega-3 fatty acids significantly improved both subjective and objective measures of dry eye. These studies primarily enrolled younger patients (mean age of 40), and authors acknowledged that further evaluation of treatment is necessary. Application to elderly patients may not be evidence-based, but adverse effects appear to be minor.

Larger trials of at least 1,000 patients evaluating dietary supplements in cataracts have included a fair number of patients over 65. Researchers in the Age-Related Eye Disease Study (AREDS), the Clinical Trial of Nutritional Supplements (CTNS), and the Carotenoids in the Age-Related Eye Disease Study have investigated antioxidants and multivitamins in relation to incidence or progression of lens opacities. Investigators in the largest study, AREDS, reported no effect with high doses of vitamin C, vitamin E, and beta carotene on the development of any type of lens opacity. Results of a later study, CTNS, demonstrated an 18% reduction of the development or progression of lens opacities with intake of a multivitamin supplement. There is some evidence to suggest higher dietary lutein and zeaxanthin may reduce the risk of developing nuclear cataract. With conflicting results, pharmacotherapy is not recommended.

Other large studies have demonstrated a reduced occurrence of age-related macular degeneration with concurrent intake of vitamins C and E, beta carotene, copper, and zinc. The AREDS, Blue Mountains Eye Disease Study, and other similar studies of age-related macular degeneration included 2,400 to 4,170 patients.
with either double-blind,\textsuperscript{17} case-control,\textsuperscript{32} or prospective cohort designs.\textsuperscript{33,34} The average age of participants in these trials was at least 65. Results of 10-year follow-up of the AREDS study demonstrated a continued significant reduction in the incidence of advanced AMD, neovascular AMD, and moderate vision loss.\textsuperscript{35}

Higher dietary or supplemental intake of lutein, zeaxanthin, and zinc with or without other vitamins or antioxidants (vitamins C and E and beta carotene) reduced incidence of advanced AMD.\textsuperscript{17,34} Although some initial evidence suggested lutein and zeaxanthin decreased risk of developing AMD, newer studies contradict this. Over 1,600 patients with an average age of 74 were enrolled in a follow-up to the AREDS study, the AREDS2 study.\textsuperscript{36} They took the original or reformulated AREDS supplement and were randomly assigned to receive a combination of lutein plus zeaxanthin, omega-3 fatty acids (docosahexaenoic acid plus eicosapentaenoic acid), both, or placebo.\textsuperscript{37} Although all patients were at risk for worsening AMD, there was no significant reduction in the incidence of advanced AMD with these additional agents.

Treatment with vascular endothelial growth factor inhibitors has been studied for more advanced macular degeneration. In patients with an average age of 77, ranibizumab decreased neovascularization and improved or maintained visual acuity in over 90% of patients compared to 62% or less in the control group.\textsuperscript{38} In a pair of rigorous studies comparing bevacizumab with ranibizumab, where the average age of participants was at least 78, changes in visual acuity were assessed to be noninferior, although some results were inconclusive.\textsuperscript{39,40} Preservation of visual acuity has also been reported in patients with mean ages of 75 to 77 treated with pegaptanib.\textsuperscript{41} These studies demonstrate lasting effect with continued treatment over a 2-year period. The ideal administration schedule of these injections is unclear. Whether injections should be given on a monthly basis or given as needed based on objective worsening of AMD has been studied, but data have not produced clear and convincing results.

**Common Problems Encountered When Treating Elderly Patients with These Conditions**

Eye drop containers may be difficult to handle for an elderly person trying to administer the solution. Older patients, especially those with lower visual acuity, have greater difficulty opening and administering eye drops than younger patients.\textsuperscript{42} In one study, 42% of patients were observed to have difficulty with instilling eye drops.\textsuperscript{43} The pharmacist should instruct patients on proper administration technique, which includes pulling down the lower eye lid with one hand and steadying the other hand that is holding the bottle against the forehead. To prevent some systemic absorption, the patient should apply pressure on the tear duct in the corner of the eye after administration of eye drops. Mobility impairments, such as tremor, arthritis, or paralysis, also make it difficult for patients to administer these medications. There are aids to help with squeezing and holding bottles so that placement of eye drops is accurate. The pharmacist has a unique opportunity in the community setting to assess a patient's ability to self-administer eye drops. In settings where eye drops are administered by a healthcare professional, such as a long-term care facility, the pharmacist should periodically observe administration technique by the patient and/or nursing staff.

**KEY POINT:** Instillation of eye drops is a difficult task for older patients who require aids and innovative techniques for sufficient administration.
agents. The option of using fixed-dose combination products is convenient for patients who could benefit from more than one class of medication.

Cost may also be an issue with some treatments for visual impairment. For primary open-angle glaucoma, prostaglandin analogs are more effective at lowering intraocular pressure than other agents and are typically chosen as initial therapy. If a patient can tolerate this drug class, then additional therapies may not be needed, thereby reducing drug costs. In AMD, medical costs are increased because treatments require an ophthalmologist for administration. Although bevacizumab for the treatment of neovascular AMD is an older anti-VEGF agent and less expensive, it is used off-label and may not be paid for by insurance.

Elderly patients with visual impairment may rely on caregivers to perform or communicate tasks required for daily living and medical care. However, many patients want to maintain independence. Strategies for effective communication with patients with vision loss include the use of corrective lenses, magnifying aids, large-print written material, and adequate lighting.

Communication can be challenging with someone who has hearing loss. An individual with presbycusis needs extra time to process what has been said. Speech should be clear and louder than normal but not necessarily slower. A quiet place, free from extraneous background noise, in close proximity, directly face-to-face with the patient will improve communication.

Asking the patient to repeat information will help identify whether key concepts have been understood. Rephrasing to less complicated and shorter sentences, pausing between sentences, and using written communication are all strategies to better communicate if the first attempt is unsuccessful.

A potentially under-recognized complication of hearing and vision loss is the mislabeling of a patient as cognitively impaired or depressed. Assessment tests for cognition often rely on both adequate hearing and vision, and those with impairments may not perform well. In social situations, patients with hearing or vision loss may attempt to compensate for misunderstanding information with an inappropriate response, or no response. A noted correlation with decreased hearing or vision is social isolation, depression, and cognition decline. In patients with hearing loss, the use of a hearing aid may improve cognition and mood.

**KEY POINT:** Many patients with hearing impairment rely on lip reading and facial gestures, and exaggerated enunciation or slowed speech impairs this process.

#### Pain

**Etiology, Epidemiology, and Clinical Presentation Specific to Geriatrics**

Pain is a subjective sensation that often serves as a signal of potential or actual damage to nerve fibers. Pain is classified by its onset, duration, or etiology. Acute injury or sudden onset of pain defines *acute pain*. Chronic, or persistent, pain may be initiated by an acute injury but has lasted beyond the normal healing time. Persistent pain may also arise from chronic diseases, cancer, or unknown causes and include both nociceptive and neuropathic features.

Nociceptive pain is initiated by thermal, electrical, or mechanical impulses that stimulate nerve fibers, called *nociceptors*. This type of pain may be less severe in older patients because of age-related changes in nerve fibers, but modulation of persistent pain may be impaired due to age-related declines in neurotransmitter production. Neuropathic pain is often associated with conditions such as diabetic peripheral neuropathy, postherpetic neuralgia, phantom limb pain after amputation, and central post-stroke pain. It also arises from persistent, nociceptive pain.
Regardless of etiology, neuropathic pain is often characterized by a burning, buzzing, stinging, shock-like, or deep aching pain or discomfort. The location of symptoms may vary. Peripheral diabetic neuropathic pain is bilateral and symmetrical, usually affecting the lower limbs. Postherpetic neuralgia occurs asymmetrically along a dermatome, typically weeks to months after onset of rash.

Despite adequate treatment, incidents of acute pain, or breakthrough pain, may occur. Causes of breakthrough pain include end-of-dose failure, when analgesia wanes before the next dose is scheduled; incident pain, when movement provokes pain; and spontaneous pain.

In residents of long-term care facilities, prevalence of pain ranges from about 50 to 80 percent. The most common type of pain reported in older patients is musculoskeletal. Neuropathic pain represents 10% of all pain, but prevalence increases with age. Peripheral diabetic neuropathic pain affects close to 25% of all patients with diabetes. Post-stroke pain affects 21% of patients after the first stroke. Inadequately treated pain in the elderly population leads to depression, anxiety, sleep disturbance, decreased quality of life, and reduced independence in daily living.

Assessment of the presence and severity of pain can be difficult in elderly patients. Reluctance to admit pain may be for cultural or social reasons. The most common methods of assessment are visual analog scales; numerical rating scales; verbal descriptor scales; or faces scales comprised of simple drawings of faces depicting varying levels of discomfort as described in Chapter 4. These scales may be used reliably in patients who are cognitively intact. The faces scale has demonstrated utility in patients with cognitive impairment. However, patients with advanced dementia may not express pain and will instead display behaviors such as aggression, irritability, groaning, rigidity, altered facial expressions, changes in eating patterns, or social withdrawal.

Summary of Standard Treatment in the General Adult Population

The experience of pain is subjective, and a systematic approach to assessment is needed to create a successful treatment plan. Before pharmacologic treatment begins, patients may need to be evaluated for risk of substance abuse, especially if opioids are to be used. Pain level, quality of life, mood, and sleep quality are evaluated to assess treatment efficacy in patients with persistent pain. Safety is also evaluated by noting adverse effects, drug interactions, and pharmacokinetic and pharmacodynamic parameters. Nociceptive pain can be successfully treated with typical analgesics, such as acetaminophen, NSAIDs, and opioids. Neuropathic pain is less predictably responsive to these analgesics. Alternative classes, or adjuvant drugs, such as antidepressants, antiepileptic drugs, and topical agents, have demonstrated efficacy in neuropathic pain.

The World Health Organization describes a step-wise approach to the management of cancer pain, which is often extended to other types of pain. The American Pain Society and American Academy of Pain Medicine suggest that opioids for chronic, noncancer pain be initiated on a trial basis to determine benefit. The pharmacologic approaches described in these guidelines are largely based on consensus expert opinion, knowledge of drug action, and presentation of the disease. A cautious approach is generally recommended, such as using nonopioid analgesics in mild pain and low doses of opioids in opioid-naive patients. Opioid analgesics are recommended as pain persists. Scheduling doses or using long-acting agents will provide more consistent pain relief. Short-acting opioids with a fast onset should be added for breakthrough pain, as needed. Titration to higher doses of long-acting agents should be based on the usage of as-needed doses. At any pain level, skeletal muscle relaxants, benzodiazepines, or other adjuvant drugs used for neuropathic pain are recommended.
Specific expert consensus guidelines are also available for knee osteoarthritis pain. For all patients, intra-articular corticosteroids are recommended to complement nonpharmacologic therapies, such as weight training. Other pharmacologic agents frequently recommended include acetaminophen, oral and topical NSAIDs, capsaicin, and duloxetine.

**KEY POINT:** Different opioids have similar efficacy and adverse effects when used in equipotent doses.

U.S. consensus guidelines and literature reviews for the treatment of diabetic peripheral neuropathic pain and postherpetic neuralgia describe the general approach for management of neuropathic pain. Pharmacologic treatment includes the use of tricyclic antidepressants, serotonin-norepinephrine reuptake inhibitors, antiepileptic drugs, opioids, and topical lidocaine or capsaicin (Table 14-3). General approaches to therapy include initiating at low doses, slow titration to an effective dose to avoid excessive adverse effects, switching to a different class if monotherapy fails, and addition of a different class if monotherapy demonstrates suboptimal efficacy. Efficacy of these treatments may take several weeks, and a change in therapy should not be considered until an adequate amount of time has passed.

**KEY POINT:** Combination therapy with analgesics and adjuvant drugs may be necessary to effectively manage persistent pain.

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**Review of Evidence Supporting Treatment Recommendations for Elderly Patients**

The American Geriatrics Society provides guidelines for the assessment and treatment of persistent pain in the geriatric population. Two follow-up guidelines specifically address pharmacologic management, outlining use of nonopioid and opioid analgesics. In general, studies of the treatment of persistent pain are varied with regard to underlying etiologies, pharmacotherapy, and length, and very few are conducted in elderly patients.

Initial treatment of musculoskeletal pain with acetaminophen is recommended. NSAIDs should be reserved because of the high risk of causing gastrointestinal bleeding, renal dysfunction, hypertension, and heart failure. Two studies providing evidence for the treatment of chronic osteoarthritis pain with acetaminophen in older adults used 3.9–4 g for periods as long as 12 months. The mean age of subjects was about 60 years but ranged as high as 90. Patients in both studies reported significant improvement in pain scores, but in one study, 1.9% of patients had clinically significant elevations in hepatic transaminases in the treatment arm. Opioids are recommended for moderate-severe pain, and doses should be scheduled around the clock for frequent or persistent pain. These recommendations are based on expert opinion, pharmacokinetic and pharmacodynamic data, and extrapolation of results from adult patients. A weakness of many studies is that efficacy and safety data specific to elderly participants are lacking. One placebo-controlled study evaluated controlled-release oxycodone in 133 subjects with osteoarthritis (average age 62 years with 43% of patients ≥65). Although this was only a 2-week trial, a clinically meaningful pain reduction (20%) from baseline was achieved within 1 day for the 10-mg arm and 2 days for the 20-mg arm. Statistically significant improvements in mood, enjoyment of life, and sleep when compared with placebo were evident in the 20-mg arm. However, over one-half of the patients withdrew participation, primarily due to adverse effects and dose-related ineffectiveness.

The use of adjuvant drugs in the treatment of neuropathic pain is recommended in guidelines for elderly patients. A caution against the use of the tricyclic antidepressants amitriptyline, imipramine, and doxepin is detailed in the guidelines, owing to adverse effects. In the 2012 update of
### Table 14-3. Common Treatments for Neuropathic Pain

<table>
<thead>
<tr>
<th>Class</th>
<th>Medication Examples</th>
<th>General Adult Treatment Principles</th>
<th>Geriatric Considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tricyclic antidepressants</td>
<td>Amitriptyline</td>
<td>First-line treatment. Effective doses lower than those used for depression.</td>
<td>Potential for anticholinergic adverse effects; orthostatic hypotension; sedating.</td>
</tr>
<tr>
<td></td>
<td>Desipramine</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Nortriptyline</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Anticonvulsants</td>
<td>Pregabalin</td>
<td>First-line treatment for neuropathic pain. Pregabalin has FDA-approved indication for DPNP and PHN.</td>
<td>Requires lower starting doses and slower titration. Pregabalin and gabapentin are renally eliminated and may require dose adjustments.</td>
</tr>
<tr>
<td></td>
<td>Gabapentin</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Carbamazepine</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Valproic acid</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Serotonin-norepinephrine reuptake inhibitors</td>
<td>Duloxetine</td>
<td>First-line treatment for neuropathic pain. Has FDA-approved indication for DPNP.</td>
<td>Not recommended in hepatic impairment or CrCl &lt;30 mL/min.</td>
</tr>
<tr>
<td></td>
<td>Venlafaxine</td>
<td>First-line treatment for neuropathic pain.</td>
<td>May need dose reduction in hepatic or renal impairment.</td>
</tr>
<tr>
<td>Opioids</td>
<td>Oxycodone</td>
<td>May be used as initial monotherapy or add-on therapy.</td>
<td>Adverse effects such as dizziness, sedation, constipation, and respiratory suppression are more common in the elderly.</td>
</tr>
<tr>
<td></td>
<td>Methadone</td>
<td>Also has NMDA antagonist activity.</td>
<td>Has long half-life that requires careful dose titration.</td>
</tr>
<tr>
<td></td>
<td>Tramadol</td>
<td>Also has weak serotonin reuptake activity.</td>
<td>May increase risk of serotonin syndrome when given with antidepressants.</td>
</tr>
<tr>
<td>Topical</td>
<td>Lidocaine</td>
<td>May be used as initial therapy or as add-on therapy.</td>
<td>Ease of use in elderly especially if in patch form.</td>
</tr>
<tr>
<td></td>
<td>Capsaicin</td>
<td>Useful in localized pain.</td>
<td>Causes increased burning during initial use. Should not be used in acute herpes zoster due to risk of mucosal contact.</td>
</tr>
</tbody>
</table>

CrCl, creatinine clearance; DPNP, diabetic peripheral neuropathic pain; NMDA, N-methyl-D-aspartate; PHN, postherpetic neuropathy.
the Beers criteria, use of tricyclic antidepressants in the elderly is cautioned because of concerns of hyponatremia or syndrome of inappropriate antidiuretic hormone and their anticholinergic effects. Other common oral adjuvant drugs are not mentioned specifically, but the evidence for their use comes from studies of disease states that are more common in the elderly population. These studies do not specifically include elderly patients and rarely include more than a few patients over 75. Results should be extrapolated with caution because patients with conditions common in the elderly, such as renal, hepatic, and cardiac diseases, are excluded from the studies. A summary of representative trials using adjuvant drugs for neuropathic pain is included in Table 14-4.

Topical agents are recommended for well-localized neuropathic pain. They have the advantage of few systemic adverse effects or drug interactions. Lidocaine is most commonly recommended and has demonstrated efficacy in small studies of patients with a wide range of ages.

**Common Problems Encountered When Treating Elderly Patients with This Condition**

There are often discrepancies in prevalence studies of pain in older patients because of the failure to recognize, report, or treat pain in these patients. Pain in the older population in general is not adequately treated, whether or not the patient is cognitively impaired or the pain is acute or persistent.

**KEY POINT:** Pain is often under-recognized and undertreated in elderly patients. Close monitoring and proactive approaches to dose titration will provide better management.

Patients with cognitive impairment may not be able to recall pain over a period of time, but the ability to report current pain often remains intact. Rating scales to assess pain in nonverbal or cognitively impaired patients are available but not always reliable. More on additional assessment tools is discussed in Chapter 4. Observing facial gestures, for example, during painful movements (e.g., during transfers) provides useful clues to how a patient behaves when in pain. Similarly, administering a test dose of an analgesic when pain is suspected and then observing for a decrease in pain-related behaviors may provide helpful information. Family or caregivers who closely observe these patients may be called on to report the presence of pain with relative accuracy.

**KEY POINT:** Nonverbal behaviors suggestive of pain can be observed to assist in pain management of patients with an inability to communicate. In patients with cognitive impairment, close family members or caretakers are reliable sources for assessing pain and the efficacy of pain management.

Most adverse effects of analgesics and adjuvant drugs are transient, and tolerance develops when they are used consistently. Initially, adverse effects such as sedation, dizziness, and orthostatic hypotension caused by antidepressants, antiepileptic drugs, and opioids can be made less bothersome by administering these drugs at bedtime.

Tolerance to opioid-induced constipation does not typically occur. The goal to managing constipation is prevention. Older patients are at greater risk for developing constipation because of decreased mobility or increased likelihood of taking concomitant drugs that cause constipation. A bowel regimen containing a stimulant laxative such as senna should be used in all patients receiving opioids, starting with an as-needed schedule. The dose can be titrated upward to ensure bowel movements occur every 3 days. A stool softener may be added to improve consistency of the stool and comfort for the patient.
Renal and hepatic impairment, whether age-related or due to other causes, predisposes patients to toxicities caused by analgesic and adjuvant drugs. NSAIDs can worsen renal function by causing vasoconstriction of renal arterioles. Neurotoxicity caused by opioids may rarely occur and is due to accumulation of renally eliminated active metabolites or rapid escalation of dose. Signs and symptoms of neurotoxicity include hyperalgesia, seizures, confusion, and twitching. Pregabalin, gabapentin, and duloxetine are renally eliminated and should be dosed accordingly in older patients. Duloxetine, tricyclic antidepressants, and most opioids are hepatically metabolized. Age-related hepatic impairment partially contributes to the increased sensitivity of elderly patients to the effects of these drugs. Longer intervals between doses and smaller doses of these agents are recommended for initial therapy, with careful titration to achieve pain control in order to avoid drug-related problems.84

Table 14-4. Summary of Trials of the Management of Neuropathic Pain

<table>
<thead>
<tr>
<th>Study drug(s)</th>
<th>Tricyclic Antidepressants69-71</th>
<th>Serotonin-Norepinephrine Reuptake Inhibitors72,73</th>
<th>Antiepileptic Drugs74-76</th>
<th>Opioids71,77-79</th>
</tr>
</thead>
<tbody>
<tr>
<td>Etiology of pain</td>
<td>Postherpetic neuralgia, diabetic peripheral neuropathic pain</td>
<td>Diabetic peripheral neuropathic pain</td>
<td>Postherpetic neuralgia, diabetic peripheral neuropathic pain</td>
<td>Postherpetic neuralgia, diabetic peripheral neuropathic pain</td>
</tr>
<tr>
<td>Average ages (years)</td>
<td>60–71</td>
<td>59–61</td>
<td>62–73</td>
<td>60–71</td>
</tr>
<tr>
<td>Size of individual trials (n)</td>
<td>Less than 50</td>
<td>Over 300</td>
<td>81–217</td>
<td>Less than 65</td>
</tr>
<tr>
<td>Average pain reduction from baseline (%)</td>
<td>32–66</td>
<td>45</td>
<td>33–40</td>
<td>38–63</td>
</tr>
<tr>
<td>Patients with significant pain reduction (%)</td>
<td>34–67</td>
<td>39–69</td>
<td>43–61</td>
<td>38–58</td>
</tr>
<tr>
<td>Limitations</td>
<td>Small study size, oldest demographic not represented</td>
<td>Younger patient population, studies supported by drug manufacturer, many concomitant disease states excluded</td>
<td>Pregabalin studies supported by drug manufacturer, many concomitant disease states excluded</td>
<td>Most studies used opioid in combination with an adjuvant or as a comparator arm</td>
</tr>
</tbody>
</table>
**KEY POINT:** First doses of adjuvant drugs should be given at bedtime because adverse effects, such as sedation and dizziness, will be less bothersome.

Acetaminophen is typically the first agent used in the older adult because it is relatively safe. Although it undergoes hepatic metabolism, the primary route is through sulfation and glucuronidation, processes that generally remain intact as a person ages. A literature review of adverse effects of acetaminophen revealed no consistent age-related hepatotoxicity in daily doses up to 4 g/day. However, with excess amounts of acetaminophen, the mixed function oxidase system is used for metabolism. It requires adequate glutathione to metabolize acetaminophen to an inactive compound. If glutathione is not available, a toxic metabolite is produced that causes hepatic cell necrosis. A maximum dose of 4 g per day of acetaminophen is recommended to reduce the risk of hepatotoxicity. Individuals who consume alcohol, are malnourished, or have pre-existing liver disease are at an increased risk. The Food and Drug Administration (FDA) updated labeling requirements in an attempt to better educate consumers about the risk of liver failure from consumption of multiple acetaminophen-containing products. The concern was that multiple products may be taken together, thereby exceeding the 4 g/day limit, a condition determined to increase the risk of hepatotoxicity. Therefore, the FDA required a limit of 325 mg per dosage unit in prescription combination analgesic products. Although it was not required by the FDA, the manufacturer of brand name Tylenol is now opting to recommend a maximum dose of 3,000 mg per day and change the dosing interval from two pills every 4–6 hours to two pills every 6 hours in the labeling of Extra Strength (500-mg) acetaminophen products. This often causes confusion among healthcare professionals regarding what the maximum daily dose should be; however, the salient point is to avoid prescribing and usage scenarios that result in unintentional dosage combinations exceeding 4 g of acetaminophen per day.

Increased adipose tissue in the body composition of older patients is also a concern with certain drugs. Fentanyl is highly lipophilic and may unpredictably release into circulation after depositing in adipose tissue. In addition, absorption of transdermal fentanyl is highly variable, may be affected by normal changes in older skin, and is temperature dependent. Transdermal fentanyl should be reserved for patients already stabilized on an oral or intravenous opioid dose. But if necessary for opiate-naïve patients, transdermal fentanyl should always be started at 25 mcg or less. This is particularly important in the geriatric population.

Methadone and meperidine are not recommended for use in the elderly. Methadone is complicated to dose, making an already dangerous class of drugs in the elderly even more complicated. It may be of some benefit in neuropathic pain; however, it should be managed by a pain specialist. Meperidine is hepatically metabolized to an active and toxic metabolite with a longer half-life than the parent drug. The metabolite is renally eliminated, interacts with other drugs, and accumulates in older patients. Normeperidine, the active metabolite of meperidine, can precipitate anxiety, tremors, and seizures. NSAIDs cause gastrointestinal ulceration, hypertension, and renal failure and are not routinely recommended for older patients. Pregabalin and gabapentin cause edema, often dose-related and troubling in patients with heart failure. Tricyclic antidepressants and serotonin norepinephrine reuptake inhibitors cause cardiac rhythm abnormalities. In patients with comorbid conditions that predispose them to these effects, these agents should be used cautiously, if at all.

Patients cite fear of adverse effects, concerns for overdosing, and addiction as reasons for inadequate analgesia. An understanding of the etiology of pain syndromes, increased sensitivity to analgesics in older patients, and measures to prevent adverse effects will promote safer pain management. Although addiction may occur in older patients, the fear is often unfounded. Educating the patient that daily use of opioids to treat pain is not addiction and that it is similar to treating high blood pressure with an antihypertensive drug will help to allay this concern.
Case 1: Outpatient Ophthalmology Clinic

Subjective:
TP is a 71-year-old Hispanic woman who presents with a progressive loss of field vision and no headache or pain.

Past Medical History:
Hypertension and chronic atrial fibrillation.

Medications:
Hydrochlorothiazide 25 mg daily, metoprolol succinate 50 mg daily, ASA 81 mg daily.

Objective:
BP 134/64 mmHg, P 58 BPM, IOP 28 mmHg (normal: 10–22 mmHg).

Assessment:
TP has open-angle glaucoma with elevated IOP with vision loss.

Plan:
Initiate therapy with latanoprost eye drops for open-angle glaucoma.

Rationale:
Prostaglandin analogs are a first-line treatment for open-angle glaucoma as well as beta blockers. Topical beta blockers would not be a first choice in this patient because she has a low heart rate due to the beta blocker therapy for atrial fibrillation.

Case Summary:
TP is at risk for glaucoma secondary to age and Hispanic ethnicity. She presents with symptoms of open-angle glaucoma (loss of field vision). Closed-angle glaucoma is uncommon and typically presents as an acute worsening of vision with associated eye pain or headache. Because there are two first-line agents for open-angle glaucoma, concomitant diseases and ease of use must be carefully considered in an elderly patient. Although administered topically, beta blockers may have some systemic absorption, which would be additive to an oral beta blocker. Latanoprost is dosed once daily in the evening, which improves compliance.
Case 2: Outpatient Pain Clinic

Subjective:
LM is a 77-year-old man with chronic nonmalignant back pain presenting with worsening pain that he describes as dull and aching. Until recently his pain had been very well managed (3/10 visual analog score) with hydrocodone/acetaminophen and occasional ibuprofen but now requires more frequent doses (up to maximum prescribed) with little added benefit.

Past Medical History:
Hypertension, obesity, obstructive sleep apnea, back pain. Back surgery 8 years ago to repair a bulging disc.

Allergies:
NKDA.

Medications:
Hydrochlorothiazide 25 mg daily, hydrocodone/acetaminophen 10/325, 2 tabs five to six times daily, ibuprofen 600 mg three to four times daily, docusate 200 mg twice daily.

Social History:
Retired from construction work. Lives with wife of 45 years.

Objective:
Ht 5’8˝, Wt 265 lb, visual analog score 7/10, BP 154/70 mmHg, P 87 BPM, BUN 25 mg/dL, serum creatinine 1.4 mg/dL.

Assessment:
LM is experiencing worsening pain that may have components of neuropathic pain and is not controlled with his current regimen. His daily dose of acetaminophen exceeds maximum recommendations.

Plan:
1. Start oxycodone extended-release 30 mg every 12 hours, change hydrocodone/acetaminophen to 1–2 tablets every 6 hours, as-needed dosing (maximum daily acetaminophen limited to 4 g), discontinue ibuprofen, and add gabapentin 200 mg at bedtime for 3 days, then increase to 200 mg twice daily.
2. Add senna as needed for opioid-induced constipation. Consider docusate in addition to senna according to patient needs.
3. Counsel patient and spouse to observe for worsening sleep apnea with addition of long-acting opioid and gabapentin.

Rationale:
LM has a history of a bulging disc and surgery on his back, has persistent pain that is worsening, and has neuropathic features. LM should be placed on a consistent opioid regimen and an adjuvant drug for his neuropathic pain. There is ample evidence to suggest how much opioid he requires, and an equivalent regimen of a long-acting opioid can be created using an equipotent dose, adjusted for possible incomplete cross tolerance and renal function. The combination of hydrocodone/acetaminophen is appropriate for moderate breakthrough pain as long as the patient does not take excessive amounts of acetaminophen. Ibuprofen should be discontinued due to its adverse effect on blood pressure and renal function. Gabapentin is a reasonable choice for the neuropathic symptoms as long as the dose is adjusted based on renal function. Although LM has not complained of constipation, a stimulant laxative should be made available with the initiation of scheduled opiate therapy to be proactive. Finally, older
patients frequently have comorbidities that require more intense monitoring or careful titration. Patients with obstructive sleep apnea are at an increased risk for respiratory depression from sedatives and pain medications.

**Case Summary:**

This patient requires multiple interventions because pain is not sufficiently responding to increased doses of analgesics. The analgesic drugs LM currently takes could potentially lead to renal and hepatic toxicity, as well as increasing blood pressure, if they are continued at a higher frequency. Other classes of analgesics and adjuvant drugs should be considered for better management of this pain syndrome.
Clinical Pearls

- Patients with cognitive impairment may be resistant to receiving eye drops. Techniques for administering eye drops to an uncooperative patient include having the patient lay back or sit in a chair with head back, explaining the process and the expected sensation of the eye drops in the eye, and pulling down the lower lid to expose conjunctiva to where the drops are to be applied. If this is unsuccessful and the patient remains with closed eyes, applying the drop to the inner corner of eye will allow the drop to fall in the eye when the eyelids are opened.

- The effective dose of tricyclic antidepressants for neuropathic pain is often less than the dose used for depression. Desipramine and nortriptyline have less anticholinergic activity than other tricyclic antidepressants and are preferred over amitriptyline in the elderly patient but should still be limited to doses of 25–50 mg/day.

Chapter Summary

Visual and hearing impairment are commonly linked with aging. Patient age is a risk factor for many causes of decreased visual acuity. Guidelines for treatments are developed from studies that contain many elderly patients. In elderly patients, however, maintenance of quality of life is just as important as managing the disease state. The pharmacist should consider quality of life when recommending therapy and ensure adequate communication techniques when interacting with patients.

Pain management recommendations in the elderly are largely based on expert opinion and knowledge of pain syndromes and the altered pharmacokinetics and pharmacodynamics of drugs in elderly patients. Pain is a subjective disease in which patients will direct therapeutic decisions by rating their pain and pain reduction. However, in elderly patients, therapeutic choices must be more conservative.

Treatments for neuropathic and nociceptive pain have a high rate of adverse effects, such as sedation, dizziness, confusion, respiratory suppression, and constipation. Many effects are transient, but older patients should begin treatment at lower doses or with longer intervals between doses in order to lessen these effects. A balance must be achieved between conservative dosing and sufficient pain management in elderly patients.

Self-Assessment Questions

1. Why does the prevalence of glaucoma increase in patients over the age of 65?
2. What age-related changes contribute to the development of dry eyes?
3. What are the two general mechanisms of action in the pharmacotherapy of open-angle glaucoma?
4. Which common drug classes in the elderly increase the risk for developing cataract?
5. Which types of visual impairment have pharmacologic prevention strategies?
6. Why are elderly patients more at risk for developing drug-related causes of hearing impairment?
7. What common disorders in elderly patients make administration of eye drops more difficult?
8. What behavior should be avoided when communicating with a patient with presbycusis?

9. What are the most common causes of pain in elderly patients?

10. What methods can be used to assess pain in patients with cognitive impairment?

11. Which drugs would not be considered first-line choices in the treatment of neuropathic pain in elderly patients?

12. How do pain management guidelines for adult and elderly patients differ?

13. What physiologic age-related changes should be considered when designing a pain regimen for an elderly patient?

14. What points of education are important when counseling a patient and caregivers about the treatment of pain?

15. Which adverse effect of opioids should be managed with another class of drugs?

16. In what disease states should pregabalin and gabapentin be used with caution?

References


Sherwood MB, Craven ER, Chou C, et al. Twice-daily 0.2% brimonidine-0.5% timolol fixed-combination therapy vs monotherapy with timolol or brimonidine in patients with glaucoma or ocular hypertension. *Arch Ophthalmol.* 2006;124:1230–1238.


Learning Objectives

1. Identify differences in the presentation and risk factors of common musculoskeletal disorders and pressure ulcers in older adults.

2. Apply evidence to support age-adjusted therapies for common musculoskeletal disorders and pressure ulcers.

3. Recommend appropriate nonpharmacologic and medication therapy to achieve treatment goals for common musculoskeletal disorders and pressure ulcers.

4. Resolve pharmacotherapy-related problems unique to older adults with musculoskeletal disorders and pressure ulcers.

Key Terms and Definitions

**BIOLOGIC RESPONSE MODIFIERS (BRMs):** Products that modulate the activity of immunologic substances such as monoclonal antibodies, cytokines, or colony stimulating factors.

**DEBRIDEMENT:** Removal of nonliving tissue from pressure ulcers, burns, and other wounds. *Sharp debridement* is a form of selective debridement where surgical instruments are used to remove specific areas of necrotic tissue. *Enzymatic debridement* is a nonselective technique that employs the use of enzyme gels placed into the wound.

**FRICTION:** Force resisting the relative parallel motion of solid surfaces. As a risk factor for pressure ulcers, this term refers to stress on the skin surface caused by sliding a patient across bed sheets.

**NUTRACEUTICAL:** Nutritional product that claims to have, in addition to nutritional benefits, medicinal effects.

**PRESSURE:** The force per unit area applied in a direction perpendicular to the surface of an object. As a risk factor for pressure ulcers, this refers to the downward pressure of the body against the surface of a bed or chair.
SHEAR: The stress applied in a direction parallel to the surface of an object. Somewhat different from friction, this refers to the stress on the internal layers of skin and soft tissue caused by shifts of internal structures. For example, when raising the head of a bed without providing assistance in repositioning, the skin of the back is pulled slightly upward while gravity pulls the ribcage and internal structures downward.

Introduction

Mobility is very important to older adults and can represent the difference between independent and assisted living. Aging is associated with changes in muscle, joint, and bone physiology and function that ultimately lead to musculoskeletal diseases such as osteoarthritis, osteoporosis, and polymyalgia rheumatica, all of which have higher incidences in older adults. Prevention can help eliminate or delay the onset of these conditions. For many older adults, these conditions require treatment, which usually provides only symptom relief, slowing of disease progression, or both, but not disease cure. Healthcare providers have an important role in promoting and encouraging healthy lifestyle behaviors for older adults, preventing disease development, assessing and identifying disease at early stages, and prescribing and monitoring age-adjusted therapies. Lifestyle adjustments are key prior to diagnosis and as a component of functional disease adaptation. Prevention and intervention can improve older adult quality of life and reduce older adult and societal healthcare costs.

Falls

Etiology, Epidemiology, and Clinical Presentation Specific to Older Adults

Falls and their consequences are serious health issues for older adults because they can decrease quality of life, lead to loss of independence, and sometimes result in death. They also create a challenge for healthcare providers and caregivers because of their multifactorial nature and complexity. Falls are either provoked (e.g., push, syncope, seizure related, icy walkway) or unintentional/unexpected (e.g., loss of balance, weakness) with the latter type being the focus of this section. Risk factors are related to patient characteristics, disorders, medications, and the environment (Table 15-1). Most of the medications associated with falls have a central nervous system effect. Medications can also induce falls through effects on blood pressure, glucose concentration, electrolytes, vision, gait, balance, and muscle weakness.

About a third of older adults residing in the community and 50% to 75% of nursing home residents experience at least one fall every year. In 2011, falls resulted in 2.4 million emergency department visits and 689,000 hospitalizations. Health expenditures for falls are significant (2005 data: $349 million for fatal falls and $8.45 billion for nonfatal fall hospitalizations).

Injuries from falls range from minor to severe and sometimes precipitate nursing home residency. Moderate to severe injury occurs in about 20% to 30% of falls, most notably lacerations, head trauma, and fractures. In older adults, 3% to 12% of falls result in a fracture, and less than 1% result in a hip fracture. Ten to twenty percent of falls occurring in the nursing home result in serious injury, resulting in a fracture 2% to 6% of the time. After hospitalization for a fall, 51% of the patients were discharged to a skilled nursing facility, 6% to home with assistance, and 5% to an inpatient rehabilitation facility. Men, whites, and non-Hispanics have a higher mortality rate after a fall. Unintentional injury was the ninth leading cause of mortality for older adults in 2010. After a fall, patients can become fearful of subsequent falls, resulting in restricted mobility, social isolation, depression, and further balance and strength deficits.

Assessment of patients with falls begins with a history, gait and balance evaluation, and
routine physical examination, progressing to multifactorial assessments and more complex mobility tests. Simple tests such as the Timed Up and Go (described in Chapter 4) and observation of gait and balance can easily be done in the clinic, whereas other more complex assessments require an occupational therapist, physical therapist, or both. A complete medication assessment, including over-the-counter (OTC) medications, herbals, and supplements should be conducted. Patients with osteoporosis are more likely to fracture after a fall; therefore, a dual energy x-ray absorptiometry (DXA) test should be performed. A 25-hydroxy vitamin D (25(OH) vitamin D) level could be ordered to evaluate for vitamin D deficiency–related muscle weakness, gait abnormalities, and decreased strength. Other tests ordered will be based on the specific comorbidities and medications.

### Table 15-1. Fall Risk Factors

<table>
<thead>
<tr>
<th>Patient Characteristics</th>
<th>Disorders</th>
<th>Medications</th>
<th>Environment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Advanced age</td>
<td>Cognitive impairment</td>
<td>Antidepressants</td>
<td>Throw rugs</td>
</tr>
<tr>
<td>Female sex</td>
<td>Depression</td>
<td>Benzodiazepines</td>
<td>Poor lightning</td>
</tr>
<tr>
<td>Walking assistance devices</td>
<td>Stroke</td>
<td>Sedative hypnotics</td>
<td>Loose electrical cords</td>
</tr>
<tr>
<td>(e.g., walker)</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Decreased ADLs</td>
<td>Parkinson disease</td>
<td>Antipsychotics</td>
<td>Steps</td>
</tr>
<tr>
<td>Alcohol use</td>
<td>Muscle weakness</td>
<td>Anticonvulsants</td>
<td></td>
</tr>
<tr>
<td>History of falls</td>
<td>Gait and balance difficulties</td>
<td></td>
<td>Pain medications</td>
</tr>
<tr>
<td>Poorly fitting footwear</td>
<td>Vision difficulties</td>
<td></td>
<td></td>
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<tr>
<td>Nocturnal voids</td>
<td>Peripheral neuropathy</td>
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<td></td>
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<tr>
<td></td>
<td>Mobility problems</td>
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<tr>
<td></td>
<td>(e.g., arthritis)</td>
<td></td>
<td></td>
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<tr>
<td></td>
<td>Cardiovascular diseases</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>(e.g., syncope, orthostatic hypotension, arrhythmias)</td>
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</tbody>
</table>

ADLs, activities of daily living.

A multifactorial and multidisciplinary approach to evaluate and resolve falls risk using nonpharmacologic and pharmacologic interventions should be employed to prevent falls (Figure 15-1). An interprofessional team of physicians, other healthcare professionals, and community members (patients, family members, older adult centers) can decrease the number of serious falls, pain, immobility, emergency department visits, and healthcare costs. Each medication, especially psychoactive medications, should be evaluated for need, lower dose, and/or safer alternatives including nonpharmacologic interventions because these changes can decrease falls risk. The guideline recommends 800 units vitamin D for those at risk for falls or with proven or suspected vitamin D deficiency. The majority of studies and meta-analyses documented a 14% to 17% decrease in falls with vitamin D therapy of 700–1,000 units daily. Lack of effect might be related to study design (differences in

### Review of Evidence Base Supporting Treatment Recommendations for Older Adults

A comprehensive falls guideline with resources is accessible on the American Geriatrics Society website. It describes patient assessment, interventions, and education and evaluates quality of available data. As part of the National Patient Safety Program, The Joint Commission created fall reduction goals (number 9, 2014) for home care and long-term care facilities related to patient assessment, patient harm reduction, and program evaluation.
patient sample, dose, vitamin D status at baseline, or both).

**KEY POINT:** Because of the multifactorial causes of falls, interprofessional team care is often beneficial in resolving fall problems.

Lifestyle and environmental changes are also effective.\textsuperscript{2,9} Exercises to strengthen muscles and improve balance, such as tai chi, should be suggested.\textsuperscript{9,13} Older adults should be encouraged to wear their glasses and use their hearing aids. As patients lose weight and height, appropriateness of footwear and assistive devices should be re-evaluated and adjusted or replaced as needed. The patient, family members, or a healthcare provider can do a home safety assessment and make adjustments to correct problems. Although hip protectors do decrease fractures from falls in nursing home residents, adherence with usage is poor. Bedrails can be appropriate in select cases, but other restraints should be avoided because they do not decrease falls and can cause death.\textsuperscript{5}

The impact of various fall intervention programs has been evaluated by many meta-analyses with mixed evidence for effectiveness of both single strategies and multifactorial interventions.\textsuperscript{2} Fall prevention can decrease injury. Absolute elimination of falls is often not an achievable goal, and not all intervention programs are practical or cost effective. Thus, interventions should be individualized to the specific patient’s needs and causes of falls and implemented following an approach similar to Figure 15-1.\textsuperscript{11} Older adults at high risk for falling might benefit from a referral to a falls clinic or program.

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**Figure 15-1.** Multifactorial approach to minimizing or eliminating falls.

Common Problems Encountered When Treating Older Adults with This Condition

Determining if the fall risk is from a medication or treated condition can be difficult. One risk factor modification at a time should be made to determine cause. Slow discontinuation of medications with a high fall risk should be tried, especially if the reason for use is unclear or no longer valid. To determine benefits and risks of a medication discontinuation, patient and caregiver follow-up is required, sometimes lasting weeks to months. Adverse medication withdrawal reactions can be precipitated by well-meaning medication reduction attempts if not done correctly.

**KEY POINT:** A thorough patient history is required to assess the contribution of medications to fall risk. Medication changes should be made slowly, one drug at a time, followed by careful observation of the results.

Limited functional status and harm from a fall create barriers to independent living and timely medical attention. Many older adults live alone, making it more complicated to seek help after a fall. An older adult can wear a device that triggers medical assistance, such as a Lifeline, that can be pressed after a serious fall for medical help to come to the home. Periodic checks from relatives and friends can also be an informal yet important mechanism for ensuring continued home safety. If a person lies on the floor too long, a pressure ulcer can occur. More serious complications related to delays in medical attention include dehydration, rhabdomyolysis, and renal failure.

Useful patient and provider information on falls and fall prevention are available from the Centers for Disease Control and Prevention, the American Geriatrics Society, and the Health Foundation for Western and Central New York. Their websites include toolkits with a variety of healthcare provider information, such as assessment tools and information on risks and medications and consumer or patient education materials, such as a home safety self-assessment tool that healthcare providers can give to patients and caregivers.

Osteoarthritis

Etiology, Epidemiology, and Clinical Presentation Specific to Older Adults

OA is the most common musculoskeletal condition and is due to an imbalance in cartilage homeostasis. Biomechanical factors, such as weight bearing responsibilities, repetitive use, and injury; genetic predisposition; and metabolic factors such as cartilage degradation impacted by interleukin-1, tumor necrosis factor-alpha (TNFα), and other pro-catabolic cytokines, contribute to the condition. Hands and knees are the most commonly affected joints, followed by hips and other smaller joints. OA risk factors include advancing age, increased weight, heredity, overuse or repetitive use of a joint, joint injury, lack of physical activity, and nerve injury. When obtaining medical histories, healthcare providers should ask about past events that can lead to OA, such as history of contact sports, motor vehicle accidents, and occupations with repetitive joint use or heavy lifting.

Increasing OA prevalence is a worldwide dilemma. Over 22% of adults over the age of 18 have self-reported doctor-diagnosed OA. This prevalence increases to 50% over the age of 65 years. The prevalence of hand OA is 43%, knee OA is 24% (which has a higher prevalence in women [27%] than in men [21%]), and hip OA is 11%. As the older adult population increases in the United States, the prevalence and impact of OA on function and healthcare costs will continue to increase. Female sex, being overweight, older age, smoking, inactivity, lower education levels, and black or white non-Hispanic origin are all associated with higher OA incidence and functional limitations. The prevalence of arthritis-associated activity limitations is over 40% in the
OA has a significant impact on function, social activities, sleep, and quality of life, especially for older adults. It typically has an asymmetric presentation as opposed to rheumatoid arthritis, which is symmetrical. OA pain typically worsens with use and improves with rest. Morning stiffness is common, typically lasting less than 30 minutes. Stiffness can also occur with extended inactivity. Pain in the joint at night and joint crepitus are other common signs. Over time, joint instability, joint enlargement, and limited range of motion (ROM) can develop. These joint changes and instability increase the risk of falls in older patients, who often already have several other fall risk factors. No laboratory markers exist for OA. Radiographic imagining with x-ray, computed tomography scan, and magnetic resonance imaging (MRI) can assist with diagnosis and monitoring of OA treatment. 

Summary of Standard Treatment

The goal of therapy is to maintain function and manage pain. Assessment of OA impact on ADLs is required and helpful with treatment decisions. OA treatment includes nonpharmacologic and pharmacologic therapies. The American College of Rheumatology (ACR) provides OA treatment recommendations based on evidence and patient preference for the most common affected joints (hand, knee, and hip). For older adults, special emphasis is placed on nonpharmacologic and topical single or combination therapy to avoid side effects. 

Nonpharmacologic treatment of hand OA includes assistive devices to facilitate ADLs, splints for the trapeziometacarpal joint, thermal modalities, and patient instruction on joint protection techniques. Thermal treatments can include heat (wax or paraffin) or cold therapy. Conditionally recommended pharmacologic therapy includes topical or oral nonsteroidal anti-inflammatory drugs (NSAIDs), topical capsaicin, or tramadol. For knee OA, nonpharmacologic treatments with strong recommendations include weight loss and cardiovascular and strengthening exercises either on land or in the water. Other nonpharmacologic therapies (tai chi, transcutaneous electrical nerve stimulation) exist with conditional recommendations. In the older adult population, social isolation can deter joint movement and exercise, so the psychosocial interventions also can be of great importance. Pharmacologic knee OA treatments include acetaminophen, oral or topical NSAIDs, tramadol, and intra-articular glucocorticoid injections alone or in combination. Current evidence does not support use of intra-articular hyaluronates, duloxetine, or opioids. These agents should be saved for patients who have failed other treatment combinations or in whom surgical interventions and NSAIDs are not options.

As with knee OA, nonpharmacologic treatment recommendations for hip OA include weight loss and land or aquatic cardiovascular and strengthening exercises. Other nonpharmacologic options with conditional recommendations are self-management programs, physical therapy with supervised exercise, psychosocial interventions, thermal modalities, and use of walking aids. Pharmacologic treatment for hip OA includes acetaminophen, oral NSAIDs, tramadol, and intra-articular glucocorticoids alone or in combination.

Nonpharmacologic therapy is an integral part of OA management. Exercise is a key component. The National Institute on Aging’s Go4Life program provides practical tips to help older adults maintain fitness and enjoy regular exercise. Exercise has several positive benefits, from function to mental health, for people with OA. Muscle strengthening around a joint with OA decreases the workload on the joint and improves joint stability. Physical therapists guide patients in the most appropriate exercises and training routines and are the best resource for assistive devices for ambulation. Occupational therapists help patients find ways to perform ADLs in spite of OA limitations. For instance, adaptive tools can assist with the use of eating utensils, hair brushes, and tooth brushes;
reaching for items on top shelves; putting on shoes; and many other ADLs. Such tools can help to maintain an older adult’s autonomy, function, independence, and quality of life. In addition, physical and occupational therapists have more advanced forms of thermal treatment available for joint pain relief. Thermal therapy can effectively increase ROM and decrease pain.22,25

Acetaminophen is first-line OA therapy in both younger and older adults followed by NSAIDs as second line.22 Refer to Chapter 14 for a more in-depth discussion of acetaminophen and NSAID dosing. Cardiovascular, gastrointestinal (GI), and renal function influence treatment decisions.

Topical therapies are excellent options in older adults because of fewer systemic side effects compared to oral therapies.26 Topical NSAIDs are specifically recommended for hand and knee OA, with evidence of efficacy for larger joints.22 Prescription diclofenac gel or topical solution is applied four times a day but has the same warnings as oral therapy. Other NSAIDs are compounded by pharmacists for topical use. Topical salicylates pose greater risk of systemic adverse effects and are less effective than topical NSAIDs.27 Topical trolamine salicylate and topical capsaicin are conditionally recommended for hand OA.22 Capsaicin should be used only on the affected joints, with immediate and thorough hand washing following application to avoid burning and irritation of skin and eyes.

Tramadol is a weak opioid receptor agonist that also inhibits serotonin and noradrenaline. It is recommended as a pharmacologic option for hand, knee, and hip OA.22 Evidence supports tramadol used with a stronger opioid for a synergistic effect that allows for more gradual opioid dose adjustments, which would be especially beneficial for older adults.28 When prescribing tramadol for OA pain, especially in older adults, renal function should be considered to determine appropriate dose, and adverse reactions (GI, central nervous system, and falls) should be monitored.

Nutraceuticals for OA prevention and treatment, such as glucosamine, chondroitin, methylsulfonylmethane (MSM), and adenosylmethionine (SAMe), as either single agents or combination products have limited efficacy data, especially in older adults.29 None of these agents are recommended in the U.S. guidelines22 for any form of OA. Systematic reviews of glucosamine and chondroitin have demonstrated inconsistent efficacy with OA pain and function improvement.30,31 Safety and efficacy data with the European prescription product, which is a different formulation from the U.S. OTC product, might not correlate with the unregulated U.S. products. If they are used, typically in a person for whom recommended therapies are contraindicated or ineffective, the studied dose of glucosamine is 1,500 mg/day, and chondroitin is 1,200 mg.32 Insufficient evidence exists to support MSM or SAMe at any dose.

Glucocorticoid injections can be effective for treatment of individually affected joints, usually the larger joints.33 Temporary synovitis can occur but frequently has a short duration. Triamcinolone hexacetonide has the greatest evidence of efficacy of the intra-articular glucocorticoids.34 Repeated injection of the same joint could increase risk of systemic side effects and joint erosion; however, the maximum number of injections per year is not defined. Good aseptic technique is critical to avoid infection. For a patient awaiting knee or hip arthroplasty, glucocorticoid joint injections provide temporary pain relief, and physical therapy improves muscle strength to aid in surgical recovery and rehabilitation.33 In this instance, the risk of deep infection following arthroplasty should be carefully considered prior to injection.

Hyaluronic acid injections received a neutral recommendation for knee and hip OA because of a lack of data and a negative recommendation for hand OA.22,35 A conditional recommendation is made for older adults in whom arthroplasty and other treatments have failed or are not options. Acid injections are well tolerated, and the primary adverse effects are a small inci-
Evidence of local injection site pain and swelling. Hyaluronic acid may have a disease modifying effect. Data are limited with prolonged use.

Opioids are reserved for severe OA pain significantly impacting daily function and quality of life for which other treatments have been ineffective. Opioids have significant adverse effects, especially pertinent in older patients with OA, and can increase falls and safety risks.

Joint replacement is effective in many patients but costly and is most often reserved for failure of nonpharmacologic and pharmacologic interventions. Data support physical therapy, exercise, and muscle strengthening prior to joint arthroplasty and resumption of activity within a day after the arthroplasty. Delayed time to ambulation and physical therapy after surgery significantly increased length of stay and recovery times.

Review of Evidence Base Supporting Treatment Recommendations for Older Adults

The most recent evidence for OA treatment in older adults focuses on prevention of harm while providing pain relief, maintaining function, and possibly slowing if not reversing some of the joint damage. Acetaminophen and topical NSAIDs are first-line for older adults because they are effective, relatively safe, and affordable compared to alternate treatments. If liver function is normal and no contraindications exist, acetaminophen should be started on a scheduled basis. The Food and Drug Administration (FDA) warns about rare but serious skin reactions (Stevens Johnson syndrome, toxic epidermal necrolysis, and acute generalized exanthematous pustulosis). For patients over age 75 or with contraindications to NSAIDs, topical NSAIDs are recommended.

Exercise has many positive benefits for people of all ages. Benefits that are particularly important for older adults include improved cognition, bone density, balance, well-being, self-care, weight loss, and decreased inflammation and risks of comorbidities.

Some evidence supports maintaining therapeutic vitamin D concentrations as a means to prevent OA. Because maintenance of serum 25(OH) vitamin D concentrations at least above 20 ng/mL may have a positive benefit on OA progression and other benefits in older adults, attention to this therapy is warranted.

Some data among older populations suggest that acceptance of different intervention strategies may vary among different groups. Older African American people with OA may be more reluctant to pursue joint arthroplasty and may respond better than Caucasian counterparts to self-management programs with instruction on techniques to manage symptoms. Therefore, patient preference should be understood when designing a treatment plan requiring long-term adherence.

**KEY POINT:** When evaluating older adults with OA, consider their medical history, especially GI and cardiovascular conditions, renal function, medication history, and risks before choosing to use an oral NSAID or a COX-2 inhibitor.

**Common Problems Encountered When Treating Older Adults with This Condition**

In older adults, nonspecific symptoms and unusual symptom presentations are more common, making evaluation of pain control and medication adverse effects even more difficult. Sometimes pain can be expressed as a decrease in eating, more sadness or depression, or behavioral problems, especially in individuals with cognitive impairment. Based on the OA therapy used, regular evaluation for GI bleed and ulceration, renal and hepatic function, and cardiovascular assessment are imperative.

Self-medication is common in OA treatment, which can lead to under- and overuse of medication. Thus, when working with older adults, specific questions related to both prescriptions obtained through multiple providers and nonpre-
scription medication therapy should be included in the medication history. The acetaminophen dose from all sources, including opioid and OTC combination products, needs to be added together to determine safety. If the older adult has concomitant hepatic impairment, acetaminophen intake should be limited or an alternative therapy selected. Patients should be screened for ethanol consumption prior to recommending chronic acetaminophen therapy, and the dose should be decreased in anyone with regular or excessive ethanol consumption.46

The nonselective NSAIDs pose GI ulcer and bleeding risks, especially in older adults. Major risks associated with ulcer formation are age over 65 years; history of peptic ulcer disease or upper GI bleeding; and concomitant medical conditions such as cardiovascular disease, diabetes, and renal or hepatic dysfunction.37 Concomitant use of glucocorticoids, antiplatelet agents, anticoagulants, tobacco, and ethanol further increases the risk for ulcers and bleeding. Older adults with GI ulcers secondary to NSAIDs do not always present with the typical symptoms, so other assessments are required.47 Use of proton pump inhibitors (PPIs) with NSAIDs can decrease GI ulcer risk but also increase therapy cost.21,22 H₂-antagonists or antacids do not adequately reduce NSAID GI ulcer risk. Refer to Chapter 14 for a more detailed review of NSAID risks and monitoring parameters.

Cost-effectiveness studies have indicated a benefit using cyclooxygenase-2 (COX-2) inhibitors in patients over age 65 years requiring NSAIDs due to decreased GI toxicity and associated costs. However, COX-2 inhibitors have cardiovascular and renal risks at least as concerning as other NSAIDs.37 NSAIDs can increase blood pressure, worsen heart failure, precipitate renal insufficiency, and increase risk of myocardial infarction through their impact on the renal collecting tubules, leading to increased fluid retention.48

Opioid use has been associated with GI adverse effects of constipation and nausea, which can also be conditions with which older adults are struggling.37 Opioids can increase cardiovascular adverse effects, pneumonia, falls, hospitalizations, and death.

**Osteoporosis and Fractures**

**Etiology, Epidemiology, and Clinical Presentation Specific to Older Adults**

Osteoporosis is a skeletal disease characterized by low bone density, decreased bone strength, and deterioration of bone micro-architecture that results in an increase in bone fragility and risk of fracture. Osteoporosis associated with aging is related more to bone formation problems than bone resorption problems, which are more associated with bone loss due to estrogen deficiency during and shortly after menopause.49 The risk factors for osteoporosis and osteoporotic fractures are similar between middle-aged and older adults50-53; however, some of these risks become more prevalent in older adults. For women, osteoporosis is generally related to estrogen deficiency and aging, whereas for men, osteoporosis is usually related to secondary causes, aging, hypogonadism, or a combination of these risks. Some of the diseases and medications associated with bone loss have higher prevalence in older adults. Risk factors for nursing home admission after a fracture or for a subsequent fracture include older age, cognitive impairment, lower bone mineral density, impaired depth perception, impaired mobility, previous falls, dizziness, poor or fair self-perceived health, malnutrition, comorbidities, inadequate social support, depression, polypharmacy, and history of inpatient delirium.54,55

Osteoporosis and osteoporotic fractures increase with aging.53,56,57 Middle-aged women have an osteoporosis prevalence of 4%, which increases to 44% to 52% in women 80 years and older.53 Whites and Hispanics have the highest incidence of osteoporosis58 and fractures even after adjusting for weight, bone mineral density (BMD), and other factors.51-53 About 50% of women and 30% of men will experience a frac-
tissue after the age of 60, which increases risk for a subsequent fracture.56,59 In white women, 75% of fractures occur after the age of 75.53 Almost all hip fractures are related to falling.56,60 More fractures occur in nursing homes than the community.54 Hip fracture incidence is decreasing, but even in 2010, 258,000 older adults were admitted to the hospital for a hip fracture.60 Although osteoporotic fractures are more common than strokes, heart attacks, and breast cancer combined and consume significant healthcare dollars ($17 billion in 2005),52 less attention is given to them. This is unfortunate because the number of patients needed to treat to prevent a second fracture is less than the number of patients needed to treat to prevent a second myocardial infarction with aspirin, statins, or beta blockers.57 Decreasing osteoporosis and hip fractures by 10% in older women and men is included in the Healthy People 2020 goals.58

Fractures can be silent or painful. They can result in decreased height, mobility, functioning, independence, and respiratory and GI function (secondary to spine kyphosis) and death. Complications following a hip fracture include fear of falling, thromboembolic events, depression, infection, subsequent fracture, pressure ulcer, poor nutrition, and death. Men,51 older adults (especially those with comorbidities),57 and nursing home residents54 have a higher mortality rate after fracture than women, younger adults, and community dwelling older adults. After hip or femur fracture surgery, 16% of patients went home and 84% went to inpatient rehabilitation, a long-term care hospital, or a skilled nursing facility, with an average stay of 36 ± 41 days.61 About 46% of the patients used home healthcare services 6 months after the fracture. One year after the fracture, 29% of the surgical patients had died and 4% to 20% still resided in a nursing home.50,52,61 Only about half of the patients with a fracture returned to pre-fracture mobility.50,54

**Summary of Standard Treatment in General Adult Population**

All older adults should be assessed for osteoporosis, starting with an annual height measurement. Overall height loss of 1.5 inches or more or annual loss of 0.8 inches or more are suggestive of osteoporosis and warrant further investigation.50 The fracture risk assessment tool (FRAX) can be used for all men and postmenopausal women 40–90 years old who have never taken osteoporosis medications or who have been off them for 1–2 years. The tool can be used for screening, diagnosis, and treatment decisions, and the results motivate patients to seek osteoporosis therapy.50-53,62 A limitation of FRAX is that not all secondary causes and risks, especially presence of falls, are included.57 The preferred osteoporosis diagnostic test is a central DXA (lumbar spine, femoral neck, total hip) with vertebral imaging sometimes recommended.50,63 FRAX and DXA are described in Chapter 4. Secondary causes should be explored with specific tests based on the condition.50-53 Each older adult should also receive a falls risk assessment and be offered interventions to prevent identified risks.2,8,11,50

Osteoporosis prevention and treatment requires a lifestyle that includes adequate calcium and vitamin D intake; exercise to improve bone strength, muscle function, and balance; minimization of alcohol and caffeine intake; no smoking; and fall prevention.9,50-53,64 Calcium alone65 does not prevent fractures. Vitamin D alone66 does not significantly influence bone density. After reanalysis of past studies and correcting meta-analyses, only combination calcium and vitamin D therapy prevented fractures in nursing home/assisted living residents.65 Variability exists for the desired 25(OH) vitamin D concentration, with ranges from 20 ng/mL64 to 30 ng/mL50 or greater51,52 suggested as the desired goal.

Guidelines are consistent in defining patients requiring osteoporosis therapy.50-53 The criteria for prescription osteoporosis medications are history of hip or vertebral fracture; DXA T-score less than or equal to –2.5 at femoral neck, total hip or spine; or low bone density (osteopenia) defined as a T-score between –1 and –2.5 with either the FRAX 10-year all major osteoporosis–related fracture probability 20% or higher or the 10-year hip fracture probability 3% or higher.
Guidelines assist with osteoporosis product decisions. Table 15-2 contains specific information about OTC and prescription medications for osteoporosis prevention and treatment. Sequential therapy, which is a bone formation medication (i.e., teriparatide) used first followed by an antiresorptive medication (i.e., bisphosphonates, denosumab, raloxifene), is advocated by the most recent National Osteoporosis Foundation (NOF) guideline to treat osteoporosis and prevent fractures; but teriparatide is generally not prescribed first because of its route of administration, cost, and lack of hip fracture prevention data. In practice, teriparatide is usually reserved for patients with significant bone loss (e.g., T-score less than −3.5 or fragility fracture) or patients that cannot use or tolerate antiresorptive medications. The American Association of Clinical Endocrinologists guideline ranks alendronate, risedronate, zoledronic acid, and denosumab as first-line therapy.

Combination therapy is rarely needed. Duration of therapy is not known, but limiting therapy to 3 to 5 years in older adults with low risk and 5 to 10 years for older adults with high risk is suggested by guidelines and expert opinion. Because bisphosphonates have a long duration of action, a drug holiday of 1 (risedronate), 2 (alendronate), or 3 (zoledronic acid) years can be used with the same or a different medication class started afterward. When to reinitiate therapy is unclear; however, suggestions include when bone markers increase, bone density significantly decreases, or fracture occurs.

Ibandronate, raloxifene, and teriparatide are second-line, raloxifene and teriparatide are also third-line, and calcitonin is fourth-line therapy. Although raloxifene or nasal calcitonin can be used, these medications have not shown hip and nonvertebral fracture prevention. Raloxifene is also associated with a small increased risk for fatal strokes. Infrequently, calcitonin is used for pain management after an acute osteoporotic fracture. Estrogen and bazedoxifene therapy are not used for older women for osteoporosis unless all other medications cannot be used. Men at high risk for a fracture should take an osteoporosis medication. Men with clinically significant androgen deficiency symptoms and low testosterone concentrations could receive testosterone replacement therapy, if they have no current or past prostate cancer. Testosterone has a minor effect on bone. In older men, testosterone therapy can increase cardiovascular disease and mortality, creating concern about testosterone use in this population.

An interprofessional team and a multifactorial approach to preventing and treating osteoporosis and fractures are needed, with attention to patient lifestyle, polypharmacy, home environment, provider and patient education, and patient assessment. Standards, such as the Healthy People 2020 goals and The Joint Commission standards, have been developed to ensure patients with a fragility fracture are evaluated for a secondary cause, have a DXA performed or treatment initiated, and receive follow-up after emergency department discharge. Fracture liaison teams help achieve these goals and improve prevention of second fractures.

Review of Evidence Base Supporting Treatment Recommendations for Older Adults

All bisphosphonates are indicated for postmenopausal women but only alendronate, risedronate, and zoledronic acid have indications for male osteoporosis. Denosumab and teriparatide are indicated for postmenopausal women and men at high risk for fracture. Raloxifene is indicated for prevention and treatment of osteoporosis in postmenopausal women and to decrease breast cancer risk in postmenopausal women with osteoporosis. Calcitonin is indicated in women at least 5 years postmenopause. Zoledronic acid is the only osteoporosis medication with an FDA indication for secondary fracture prevention. Some osteoporosis studies compared the older participants to younger participants and found no differences; but generally these comparisons were underpowered to evaluate age differences in bone density, fracture risk reduction, and adverse reactions. Effectiveness data in adults
### Table 15-2. Pharmacotherapy for Osteoporosis Prevention and Treatment

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dose</th>
<th>Advantages</th>
<th>Limitations</th>
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<tbody>
<tr>
<td><strong>Calcium</strong></td>
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<td>Most common</td>
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<td>salts used</td>
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<td>are carbonate</td>
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<td>(40% elemental</td>
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<td>calcium) and</td>
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<td>citrate (21%</td>
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<td>elemental</td>
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<td>calcium)</td>
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<tr>
<td>300–500 mg</td>
<td></td>
<td>Sometimes easier than ingesting foods,</td>
<td>Administration</td>
</tr>
<tr>
<td>elemental calcium</td>
<td>tablets as needed to achieve adequate intake of 1,000 mg for men</td>
<td>especially for those who are lactose</td>
<td>Dietary intake preferred.</td>
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<td></td>
<td></td>
<td>50–70 years old and 1,200 mg daily for women</td>
<td>Carbonate but not citrate products should be taken with food.</td>
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<td></td>
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<td>50 years and older and men 71 years and older.</td>
<td>Citrate tablets are more expensive and more tablets might be needed.</td>
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<td>Maximum intake from food and supplements per</td>
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<td>IOM is 2,000 mg per day but per NOF guideline</td>
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<td></td>
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<td>is 1,500 mg per day.</td>
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<td>Administration—dietary intake preferred.</td>
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<td>Carbonate but not citrate products should</td>
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<td>be taken with food.</td>
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<td>Citrate tablets are more expensive and</td>
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<td>more tablets might be needed.</td>
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<td>Adverse effects</td>
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<td>Constipation, gas, bloating, kidney stones</td>
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<td>(rare).</td>
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<td>Slight increase in myocardial infarcts and</td>
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<td>kidney stones with daily calcium use greater</td>
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<td>than adequate intakes.</td>
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<td>Drug interactions</td>
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<td></td>
<td>Proton pump inhibitors, iron, tetracycline,</td>
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<td></td>
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<td>quinolones, bisphosphonates, phenytoin, and</td>
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<td>fluoride.</td>
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<td>Food interactions</td>
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<td>Oxalates, phytates, sulfates, and fiber</td>
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<td>(variable).</td>
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<td>Administration</td>
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<td>Severe renal or hepatic failure, use different</td>
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<td>vitamin D analogs.</td>
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<td>Obesity or malabsorption conditions—potentially</td>
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<td>need higher dose.</td>
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<td>Adverse effects</td>
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<td>Hypercalcemia (uncommon).</td>
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<td>Drug interactions</td>
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<td>Phenytoin, barbiturates, carbamazepine,</td>
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<td>rifampin, cholestyramine, colestipol, orlistat,</td>
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<td>and mineral oil.</td>
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<td>Monitoring</td>
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<td></td>
<td>25(OH) vitamin D concentration; after 3</td>
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<td></td>
<td>months to assess drug therapy.</td>
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<td><strong>Vitamin D</strong></td>
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<td>More accessible than vitamin D–fortified</td>
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<td></td>
<td></td>
<td>foods.</td>
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<td></td>
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<td>Administration</td>
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<td>Severe renal or hepatic failure, use different</td>
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<td>vitamin D analogs.</td>
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<td>Obesity or malabsorption conditions—potentially</td>
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<td>need higher dose.</td>
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<td>Drug interactions</td>
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<td>Phenytoin, barbiturates, carbamazepine,</td>
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<td>rifampin, cholestyramine, colestipol, orlistat,</td>
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<td>and mineral oil.</td>
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<td>Monitoring</td>
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<td>25(OH) vitamin D concentration; after 3</td>
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<td></td>
<td></td>
<td>months to assess drug therapy.</td>
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</tbody>
</table>
### Table 15-2. Pharmacotherapy for Osteoporosis Prevention and Treatment (cont’d)

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dose</th>
<th>Advantages</th>
<th>Limitations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bisphosphonates</td>
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<tr>
<td>- Alendronate</td>
<td>10 mg daily; 70-mg tablet, 70-mg tablet with vitamin D (2,800 or 5,600 units), or 70-mg effervescent tablet weekly.</td>
<td>Reasonably safe, 7–10-year safety data. Much BMD data. Spine and hip (except ibandronate) fracture prevention data. Weekly, monthly, quarterly, and yearly administration sometimes improves adherence.</td>
<td>Administration: Check Medicare Part D plan to see what is Tier 1 and requirements for intravenous administrations. Normal serum calcium and creatinine required before intravenous therapy. Complex oral administration: Take with a full glass of water not juice, coffee, or tea and on an empty stomach. Remain upright for at least 30–60 minutes. Do not take with any other medications. Special products: Effervescent alendronate: Dissolve tablet in 4 oz plain water; wait 5 minutes for effervescence to stop, stir for 10 seconds, and then ingest 30 minutes before breakfast; other directions the same. Delayed-release risedronate: Immediately after breakfast with 4 oz plain water; other directions the same. Missed doses: If weekly, take next day; need ≥5 days between doses. If monthly, take as soon as remembered; need ≥7 days between doses. Contraindications: Renal function CrCl &lt;30–35 mL/min (controversial); if age-related renal dysfunction might be ok to use oral therapy. Absolute contraindication if CrCl &lt;30–35 mL/min or acute kidney failure for zoledronic acid. Esophageal disorders or severe GI problems (oral). Adverse effects: GI: nausea, heartburn, abdominal pain, irritation. Muscle aches and pains (uncommon); discontinue if severe. Transient (24–72 hr) flu-like symptoms with intravenous administration, can pretreat, sometimes decrease with subsequent treatments. Ulceration, perforation, and bleeding with oral therapy (rare). Osteonecrosis of the jaw and atypical fractures (rare). Drug interactions: Calcium, minerals, proton pump inhibitors, ( H_2 ) blockers, warfarin with delayed-release risedronate.</td>
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<tr>
<td>- Ibandronate</td>
<td>150 mg monthly, 3-mg intravenous infusion over 15–30 seconds quarterly.</td>
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<tr>
<td>- Risedronate</td>
<td>5 mg daily, 35 mg weekly, 150 mg monthly. 35 mg delayed-release tablet.</td>
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<tr>
<td>- Zoledronic acid</td>
<td>5 mg intravenous infusion over 15 minutes yearly for treatment and every 2 years for prevention.</td>
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</table>
### Table 15-2. Pharmacotherapy for Osteoporosis Prevention and Treatment (cont’d)

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dose</th>
<th>Advantages</th>
<th>Limitations</th>
</tr>
</thead>
</table>
| Denosumab       | 60 mg subcutaneous injection every 6 months. | Can use in patients with CrCl <30 mL/min.           | Administration: By healthcare provider.  
|                 |                                           |                                                     | Prior authorization required.  
|                 |                                           |                                                     | Normal serum calcium required before therapy.  
|                 |                                           |                                                     | Expensive.  
|                 |                                           |                                                     | Adverse effects: Dermatitis, rash/eczema, bone/muscle pain,  
|                 |                                           |                                                     | mild GI events, cystitis, other infections,  
|                 |                                           |                                                     | hypocalcemia, flatulence.  
|                 |                                           |                                                     | Osteonecrosis of the jaw and atypical fractures (rare). |
|                 |                                           |                                                     | Contraindications: Previous venous thromboembolic event.  
|                 |                                           |                                                     | Adverse effects: Hot flushes, leg cramps, myalgias,  
|                 |                                           |                                                     | thromboembolism, pulmonary embolism,  
|                 |                                           |                                                     | peripheral edema; cataracts and gallbladder disease (rare).  
|                 |                                           |                                                     | Box warning for fatal stroke. |
| Calcitonin      | 200 units intranasal daily, alternating nares every other day. | Some analgesic effect after a fracture. Also used for metastatic bone pain. | Efficacy: Only vertebral fracture prevention.  
|                 |                                           |                                                     | Administration: Refrigeration until first use.  
|                 |                                           |                                                     | Adverse effects: Rhinitis, epistaxis, nasal irritation and dryness.  
|                 |                                           |                                                     | Under review for potential increased cancer risk. |
| Teriparatide    | 20 mcg subcutaneously daily for up to 2 years. | Only product that builds new bone. Pen device for administration. | Efficacy: Limited use for 24 months.  
|                 |                                           |                                                     | Might need prior authorization.  
|                 |                                           |                                                     | Administration: Daily injection.  
|                 |                                           |                                                     | Discard pen 28 days after being opened.  
|                 |                                           |                                                     | Refrigeration required, can complicate travel.  
|                 |                                           |                                                     | Expensive.  
|                 |                                           |                                                     | Might need prior authorization.  
|                 |                                           |                                                     | Contraindications: Bone cancer, Paget disease, open epiphyses,  
|                 |                                           |                                                     | hypercalciuria, unexplained increased alkaline phosphatase, prior skeletal radiation.  
|                 |                                           |                                                     | Box warning: do not use if at risk for osteosarcoma.  
|                 |                                           |                                                     | Adverse effects: Pain at injection site, headaches, nausea,  
|                 |                                           |                                                     | dizziness, leg cramps, arthralgias,  
|                 |                                           |                                                     | transient hypercalcemia, and increase in uric acid (rare). |

CrCl, creatinine clearance; IOM, Institute of Medicine; NOF, National Osteoporosis Foundation.
75 years and older are limited but suggestive of vertebral fracture reduction with risedronate, alendronate, and teriparatide and nonvertebral and hip fracture reduction with risedronate for those 70–79 years old.\cite{57,72}

Healthcare use and costs for treating fractures are higher in older adults\cite{73} and quality of life\cite{57} is reduced after a fracture, making prevention important. Treating osteoporosis in older adults is cost effective. A well-designed pharmacoeconomic study showed that treating older adult women 65–84 years old with osteoporosis was cost effective and would even generate cost savings for adults 85 years and older with osteoporosis.\cite{74,75} Cost effectiveness could be realized for men 65 years and older with a prior fracture and men 80–85 years old with osteoporosis.\cite{76} If osteoporosis treatment is less than $500 annually (2007 dollars), treating men 70 years and older with osteoporosis would also be cost effective.

**Common Problems Encountered When Treating Older Adult Patients with This Condition**

The main challenge is to get providers to assess and treat older adults for osteoporosis. Over a 7-year period, only 31% of older white women, 15% of older African American women, and 5% of older men had a DXA test.\cite{57} In the nursing home, FRAX overestimates the need for therapy (81% using femoral neck T-score). If previous fracture and/or DXA T-score are used, 54% would need osteoporosis therapy, increasing to 73% if vertebral imaging also is used.\cite{77} Even after a hip fracture, less than 22% of older adults received a DXA or prescription therapy.\cite{57} Osteoporosis medication therapy use after a fracture varies by fracture site; wrist (14%), hip (26%), and spine (42%) with older age not influencing treatment.\cite{78}

Older adults after a fracture should be offered osteoporosis prevention and treatment therapies to enhance the remainder of life. Fracture prevention begins within 6 to 12 months of therapy for vertebral fracture prevention and 18 to 24 months for hip fracture prevention. Because the average life expectancies for older adults who are 75 years or older, nursing home residents, and assisted living residents is greater than the onset of fracture prevention, osteoporosis medications can be considered for these populations.\cite{57,77} However, some comorbidities such as a neurologically limiting stroke, advanced stage dementia, and terminal cancer generally warrant not using osteoporosis medications. Osteoporosis medications can be considered for discontinuation in some patients, especially for those patients receiving hospice care.

Patient analysis of dietary calcium intake is needed to determine safe calcium supplementation amount.\cite{58} Supplementation need is the difference between Institute of Medicine (IOM)–recommended intakes and dietary daily calcium ingestion. If daily calcium ingestion cannot be determined, the National Health and Nutrition Examination Survey average calcium intakes can be used instead, which for women is approximately 600–640 mg elemental calcium and for men is approximately 730–760 mg.\cite{79} Supplemental doses should be distributed throughout the day. Calcium supplement labels can be confusing, and some older adults will need assistance determining the calcium content of a tablet, the number needed per day, and correct use.

Calcium absorption is variable and likely lower in some older adults. Calcium carbonate but not calcium citrate requires an acid environment, which can be decreased in older adults, for disintegration and dissolution. Taking calcium carbonate with food might overcome this problem. PPI use was associated with increased fracture risk, potentially related to decreased calcium absorption from calcium carbonate products secondary to PPI decreased gastric acid.\cite{80} For older adults using PPIs, increasing calcium carbonate daily intake and taking it later in the day with food or using calcium citrate might solve this absorption problem.
Because of minimal sun exposure (residential living, sunscreen use, northern hemisphere residence), few vitamin D–supplemented foods and beverages, and kidney and liver age-related changes, older adults are at increased risk for low vitamin D concentrations or altered metabolism. Therefore, older adults usually need supplementation. Based on Markov decision analysis, universal vitamin D supplementation was similar in cost effectiveness to population screening for women and men 65 years old, but population screening for women and men 80 years old was more cost effective than universal supplementation. Although the IOM-recommended adequate vitamin D intake has been increased, one Canadian study documented that a vitamin D intake of 1,000 units per day only placed 35% of older adults in the therapeutic range (≥30 ng/mL), whereas 4,000 units per day put 88% in the therapeutic range. Because 25(OH) vitamin D levels are expensive, a cost-saving measure is to draw a 25(OH) vitamin D level after taking 800–1,000 units vitamin D<sub>3</sub> supplement daily for 3–4 months (time for biological steady state) to ascertain the need for replenishment therapy or a higher maintenance dose. Inter-assay variability exists, so patients should have follow-up vitamin D levels analyzed at the same laboratories until all assays are standardized. Various repletion dosage schedules for vitamin D insufficiency (21–29 ng/mL) exist, ranging from 800–4,000 units vitamin D<sub>3</sub> daily to 50,000 units vitamin D<sub>2</sub> or D<sub>3</sub> weekly to monthly, with daily dosing preferred over larger, less frequent dosing options. For vitamin D deficiency (<21 ng/mL), repletion dosage schedules are also variable but generally involve using 50,000 units vitamin D<sub>2</sub> or D<sub>3</sub> 1–2 times weekly for 8–12 weeks and then implementing a daily maintenance dose of 800–1,000 units or higher, as needed.

Prior to initiating bisphosphonate therapy, especially intravenous therapy, a patient’s serum calcium should be in the normal range and, if not, corrected before administration. Oral bisphosphonates require the older adult to be able to remain upright (seated or standing) for at least 0.5–1 hour after ingestion, which might be difficult for some older adults with stroke, immobility, or dementia. For patients with difficulties swallowing or with feeding tubes, effervescent alendronate could be used. If the older adult cannot tolerate oral bisphosphonates, intravenous zoledronic acid or injectable denosumab or teriparatide therapy can be instituted. With correct usage, bisphosphonates have few adverse effects. Weekly and monthly bisphosphonate oral administrations decrease serious but not common GI bisphosphonate adverse effects compared to daily use. Although oral bisphosphonates are labeled not to use if creatinine clearance is <30–35 mL/min, some but not all experts suggest bisphosphonates for 3 years for chronic kidney disease (CKD) 4 and half the dose for 3 years for CKD 5 if the patient has age-induced renal compromise and has had a fragility fracture suspected from high bone turnover (e.g., from bone biopsy). These older adults should be assessed first for normal calcium and vitamin D concentrations, and low concentrations should be corrected before initiating the oral bisphosphonate (this recommendation is not evidence based). Intravenous zoledronic acid is contraindicated for creatinine clearances <35 mL/min and with acute renal failure.

Denosumab requires a normal serum calcium concentration before use and prior authorization to determine insurance coverage. A healthcare provider needs to administer denosumab every 6 months, which can create transportation issues for product pickup at a pharmacy and a clinic administration visit; however, some pharmacies are beginning to offer administration service.

Adherence (30% to 50%) and persistence (30% to 35%) with osteoporosis medications are suboptimal, resulting in decreased medication benefits. Older adults have circumstances that lead to decreased adherence, such as increased pill burden, cognitive impairment, or limited resources. Complex product administration influences adherence;
with new and refilled prescriptions, adherence might be corrected with the teach-back patient education method. Patient counseling might overcome adherence problems related to fears about adverse effects, misunderstandings about disease severity and medication, and attitudes toward medications. Monthly medications do not always improve persistence. Intravenous and injectable therapies might present cost issues to older adults, especially if they are at or near the coverage gap of their Medicare Part D insurance programs.

Due to polypharmacy, older adults are at increased risk for medication-induced bone loss. Glucocorticoids are the most potent bone destroying medications. Although use is limited today, they were common therapies in the past before safer medications existed for such morbidities as chronic obstructive pulmonary disease and rheumatoid arthritis (RA), thereby warranting a good past medication history assessment. For patients starting or receiving glucocorticoid therapy (e.g., ≥5 mg prednisone or equivalent for ≥3 months), a baseline and follow-up hip and spine DXA and vertebral imaging are recommended. The first step of therapy is to try to eliminate glucocorticoid use or, if not possible, use the safest medications with the lowest dose for the shortest duration. A bone-healthy lifestyle and higher calcium (1,200–1,500 mg) and vitamin D (800 units or more to achieve therapeutic concentrations) intakes are required if on glucocorticoids.

Although guidelines exist for glucocorticoid-induced osteoporosis prevention and treatment, they are frequently not followed. If the FRAX major osteoporosis fracture risk score is >20% (high risk), then alendronate, risedronate, or zoledronic acid can be used. Teriparatide is also an option if the dose is 5 mg or more of prednisone (or equivalent) daily or any prednisone dose if for greater than 1 month. If the older adult is at medium risk for osteoporosis (FRAX risk score 10% to 20%) and the prednisone dose is <7.5 mg daily, then alendronate or risedronate is used, with zoledronic acid also an option if prednisone 7.5 mg or more daily. For older adults at low risk (FRAX <10%) and prednisone <7.5 mg daily, no prescription therapy is required, but if the dose is ≥7.5 mg or more daily, then alendronate, risedronate, or zoledronic acid can be used. Since the guideline was published, denosumab has been approved and has shown some efficacy to decrease glucocorticoid-induced bone loss.

Besides glucocorticoids, many other medications have bone effects. As older adults age, their levothyroxine dosage requirements frequently decrease, creating excess concentrations that can increase bone loss if dosage adjustments are not made. Thus, yearly thyroxine-stimulating hormone (TSH) levels should be drawn, with thyroid replacement doses adjusted to achieve TSH concentrations in the middle to upper normal therapeutic range. Anticonvulsant therapy with medications such as phenytoin and phenobarbital can cause both osteoporosis and osteomalacia. With long-term use of these medications, monitoring 25(OH) vitamin D concentrations might be helpful to identify and correct any vitamin D deficits. Some cancers and chemotherapies such as prostate and breast cancers and gonadotropin-releasing hormone agonists (e.g., goserelin, leuprolide) and aromatase inhibitors (e.g., anastrozole) increase bone loss and osteoporosis. Zoledronic acid and denosumab can limit this bone loss, reduce skeletal complications, and inhibit cancer cells. Selective serotonin reuptake inhibitors have been associated with decreased osteoblast function and increased fracture risk, warranting monitoring for falls and osteoporosis.

**KEY POINT:** Most patients receiving medications causing bone loss and fractures have not been educated about drug-induced osteoporosis, making additional diagnostic, prevention, treatment, patient education, and motivational strategies necessary.
Rheumatoid Arthritis

Etiology, Epidemiology, and Clinical Presentation Specific to Older Adults

RA is a progressive autoimmune disorder of unknown etiology. It is a chronic, destructive disease characterized by symmetric, erosive synovitis. Up to one-third of cases are diagnosed at age 60 or beyond, known as elder-onset rheumatoid arthritis (EORA). Compared to young-onset rheumatoid arthritis (YORA), patients with EORA might have genetic differences, in particular a decreased frequency of DRB1*04 alleles.

RA is found in approximately 0.5% to 1% of the population impacting roughly 1.3 million Americans. About 2% of people 60 years and older have RA. In working-age adults, the incidence is higher in women. After age 65 years, men and women have RA at about the same rate, but evidence in recent years suggests an increase for women. It can occur at any age but most commonly presents in the 30s to the 50s. RA is sometimes diagnosed after age 65 years. The average age of those living with it has gradually increased to 66.8 years, based on 1995 data. The mortality rate of people with RA has remained relatively stable between 1965 and 2005, whereas the mortality rate overall has declined. As available treatments advance and are able to better limit disease activity, the psychological and physical impact of RA is decreasing.

The diagnostic RA criteria are based on number and size of affected joints, rheumatoid factor and anti-cyclic citrullinated peptide antibodies (ACPA) status, duration, and inflammatory laboratory parameters. Presence of these factors is entered into a weighted scoring mechanism. A score of 6 or greater is indicative of "definite" RA in a patient with clinical synovitis with no other apparent etiology. RA affects both joints and other organ systems. Joint destruction can significantly impact daily function. Fatigue is a component that can further limit daily function. Other constitutional symptoms include malaise, fever, weight loss, depression, and weakness.

Extra-articular manifestations of RA include cardiovascular disease, anemia, interstitial lung disease, osteopenia, osteoporosis, and ocular involvement (including scleritis). Rheumatoid nodules, vasculitis, Felty syndrome, and Sjögren syndrome. The presence of extra-articular manifestations and markers of more active disease such as more involved joints, higher erythrocyte sedimentation rate (ESR), positive rheumatoid factors, and more functional impairment are all associated with higher mortality rates.

The EORA patients are more likely to have an abrupt onset with involvement of large joints such as hip and shoulder and more frequently present with constitutional symptoms. EORA patients who are seropositive tend to have a more aggressive form and require more aggressive therapy, similar to their YORA counterparts. Seronegative patients often have a disease course that mimics or coincides with Sjögren syndrome or polymyalgia rheumatica (PMR). These are often easier to manage with disease modifying anti-rheumatic drugs (DMARDs) and glucocorticoids, and this population has a higher rate of remission. EORA is a predictor of cardiovascular mortality, so aggressive cardiovascular risk reduction and management are warranted.

Summary of Standard Treatment in General Adult Population

Nonpharmacologic therapy is a key part of RA care. Exercise to maintain ROM and strength, rest, thermal modalities, weight loss, relaxation techniques, and physical and occupational therapy are all important nonpharmacologic therapy components. Therapists can aid people with RA in the use of joint braces and assistive devices to minimize functional limitations.

The 2012 ACR guideline provides detailed algorithms for RA treatment. DMARD monotherapy is recommended in early RA without poor prognostic factors. Early or established RA, features of poor prognosis, and higher disease
activity warrants earlier use of combination DMARD therapy or biologic response modifier (BRM) therapy.

The ACR guideline summarized the evidence guiding appropriate use of nonbiologic DMARDs and BRMs, which are classified as anti-tumor necrosis factor alpha (anti-TNFα) agents and other non-TNFα BRMs.97 More long-term evidence exists for the DMARDs than for the BRMs. Treatment recommendations are dependent on duration of disease activity (early RA is <6 months; established RA is ≥6 months), disease activity (low, moderate, or high), and presence of poor prognostic factors. Poor prognostic factors include one or more of functional limitations, extra-articular disease (e.g., presence of rheumatoid nodules, RA vasculitis, Felty syndrome), positive rheumatoid factor or anti-citrullinated protein antibody, or bony erosions by radiograph.

The DMARDs are used singularly or combined depending on disease activity and prognostic factors, with more aggressive therapy used with more severe RA.95 Most DMARDs take several weeks before onset of full therapeutic benefit and have limited durations of efficacy. A 3-month trial is recommended before making decisions to alter therapy with DMARDs or anti-TNFα; 6 months for non-TNFα BRMs. If monotherapy does not get and keep a patient at goal of low disease activity or remission, then addition of a different DMARD (i.e., methotrexate, leflunomide, or hydroxychloroquine) is warranted. If one to two combinations of DMARDs do not achieve and maintain the patient at goal, then the DMARD is changed to or combined with a BRM.

All BRMs can be used as monotherapy with the exception of infliximab, which should always be paired with methotrexate.97 Rituximab can be used when patients have poor prognostic factors, have failed other therapies, or who have had a malignancy within the past 5 years. Combinations of biologic therapies are not supported by current evidence.

Because DMARDs and BRMs can take weeks to months to achieve maximum effect, glucocorticoids and NSAIDs can be used for short-term pain management. Glucocorticoids differ from NSAIDs by having both disease-modifying and anti-inflammatory properties. Glucocorticoids should be used at a low dose (5 mg/day or less) for limited courses of therapy; only rarely is long-term use warranted.98 Low-dose glucocorticoids are used as adjunct therapy for pain and inflammation control or for bridge therapy while making changes in DMARD or BRM therapies. Short-term high-dose bursts can be used for acute flares. Glucocorticoids can also play an important role in withdrawal of BRM and DMARD therapy in patients in remission.99 NSAIDs can help with pain and inflammation; they do not have disease-modifying activity. Risks and benefits should be weighed, especially in patients with cardiovascular disease risks, renal dysfunction, or GI ulcers or bleeds.100 Disease activity measures help quantify current disease activity, select medication choice and numbers of agents to use, and identify when a patient is in remission.101 There are several different tools that have been validated to monitor and quantify disease activity. When a patient responds to therapy with sustained low disease activity or remission, downward titration and even removal of the BRM is supported by evidence.102,103

Review of Evidence Base Supporting Treatment Recommendations for Older Adults

Because older patients with RA have typically had the condition for many years, the disease is often further progressed, with greater impact on function. The standard RA treatment for older adults is the same as other adults, and few data are specific to older patients. Older adults respond to DMARD and BRM therapies in a way that is comparable to younger adults.104 A rapidly-administered patient questionnaire, such as the Multi-Dimensional Health Assessment Questionnaire, can be at least as indicative of treatment response and may replace more complex assessments of response that include laboratory parameters and physical examination.105
Older patients tend to have more comorbidities that can influence RA medication selection. Anti-TNFα therapies can increase risk of lymphoma.\textsuperscript{106} They should be avoided in people with a history of malignancy within the past 5 years. Anti-TNFα therapies also should not be used in patients with New York Heart Association class III or IV heart failure or with ejection fraction <50%.\textsuperscript{97} In patients with untreated hepatitis B or treated hepatitis Child-Pugh class B or higher, BRMs should be avoided. In RA patients with hepatitis C, etanercept can be used.

Prior to initiation of BRMs, all patients should be screened for latent tuberculosis (TB) infections. The tuberculin skin test can be used in most patients. If someone has a history of a positive test, the interferon-ϒ-release assays are the preferred screening test. If either test is positive, the patient should also be screened with a chest radiograph and if that is positive, then a sputum assessment. If the patient has TB, TB therapy should be completed before initiating biologic therapy.\textsuperscript{97}

Evidence supports a link between the inflammatory processes of RA and those of cardiovascular disease.\textsuperscript{107} In particular, T-lymphocytes are involved in both processes. People with RA have a higher risk of myocardial infarction, with a rate increase similar to diabetes. High-dose glucocorticoids (>7.5 mg/day) can increase blood pressure and cardiovascular risks. Anti-TNFα therapies and methotrexate might have positive benefits for both RA and cardiovascular disease.

The natural course of aging can decrease immune response. RA and associated medications can further increase the risk of infection. Glucocorticoids have increased infection and hospitalization rates when used for RA.\textsuperscript{108} When used short term at a low dose (≤5 mg/day), glucocorticoids can produce anti-inflammatory and disease-modifying effects and cause fewer adverse effects.\textsuperscript{98} At higher doses or longer durations, the significant side effect profile, especially impact on bone density, glaucoma, weight, and metabolic system, should be weighed against advantages.\textsuperscript{17,109}

Older adults with RA should receive immunizations for influenza, pneumococcus, and hepatitis B.\textsuperscript{97} For the pneumococcal vaccine, this should be given once after age 65. If the person received a prior pneumococcal vaccine before age 65, and it has been at least 5 years, that person should be revaccinated once. An older adult with RA starting DMARD therapy should be vaccinated for herpes zoster. If an older adult is already on DMARD therapy and has not been vaccinated, all vaccines can be given. If an older adult is already on any BRM, the herpes zoster vaccine is not recommended.

Medication regimen monitoring and adverse effect management are integral parts of therapy with immune modulating therapies. In particular, complete blood count, liver function tests, and renal function monitoring are important for most of these agents. Both RA and glucocorticoids are independent risk factors for osteoporosis, warranting DXA evaluations of bone density and considerations for osteoporosis prevention or treatment medications. Specific medication monitoring recommendations should be followed.

**Common Problems Encountered When Treating Older Adults with This Condition**

Older adults do not always receive RA therapy as comprehensive or aggressive as their younger counterparts. Studies of attitudes and priorities have demonstrated older adults often select therapy options with fewer daily side effects, even if there are longer-term risks.\textsuperscript{104} Rheumatologists and patients prioritize therapy considerations differently.\textsuperscript{110} Open communication about options can help patients and providers find common goals and strategies.

Fatigue is a common sequela of RA that can have a significant impact on function in older adults. Physical activity and psychosocial interventions have been demonstrated to have a benefit in helping manage fatigue.\textsuperscript{111}

RA is a progressive disease that leads to loss of muscle tone and function over time, as
does aging. So, when flares, fractures, illness, or hospitalization cause weakness, it takes even longer in older patients to regain function. Ability to perform ADLs, participation in fun activities, need for personal help and assistive devices, and transportation issues contribute to the total picture of RA care. Exercise and coordinated interventions can help maintain function, decrease pain, and enhance quality of life. Components of interventions demonstrated to have success include group education, self-management, upper extremity–focused exercise instruction, and maintenance of a home exercise regimen. Yoga and tai chi have also been shown to help maintain function and improve psychosocial aspects of RA management.

Several oral health and GI implications exist with both RA and its treatment. The temporomandibular joint is one of the joints that can be impacted by RA. Glucocorticoids and bisphosphonates can increase risk of jaw osteonecrosis. Hand and jaw RA can make it difficult for patients to practice good oral hygiene. Attention to oral care can improve oral health, quality of life, and self-esteem. Constipation is a common problem for older adults even without concomitant medical conditions. Decreased physical activity due to RA, decreased total body water, and altered nutritional and fluid intake are contributing factors. Opioids are well known for constipation as a side effect; thus, treatment benefit needs to be greater than adverse effects. If used, therapy should only be for a short period (<6 weeks) with preventative measures for constipation and fall risk employed.

With age often comes an accumulation of medical conditions with multiple implications on therapy. For instance, some older adults might not be surgical candidates, thus eliminating joint replacement as a therapeutic option. In addition, depression is common with any chronic condition, especially musculoskeletal disorders. Anemia is a common comorbidity, and the fatigue of RA and anemia further contribute to the difficulties of managing RA and other comorbidities and differentiating causative factors.

### Polymyalgia Rheumatica and Giant Cell Arteritis

**Etiology, Epidemiology, and Clinical Presentation Specific to Older Adults**

Although the exact causes of PMR and giant cell arteritis (GCA) are unknown, pathophysiology might be related to aging, the immune system, decreasing endocrine function, genetics, and environmental factors. These diseases predominantly affect older adults (>50 years) with average onset at 73 for PMR and 70 for GCA. Women and whites are more likely to develop PMR and GCA. The annual incidence of PMR and GCA is 53 and 19 patients per 100,000 people, respectively.

PMR symptoms are moderate to severe muscle aches and morning stiffness of the torso (e.g., neck, shoulders, pelvis) or upper and lower extremities that last for greater than 45 minutes and persist longer than 2–8 weeks. Patients can experience fatigue, decreased energy, weakness, weight loss, anemia, and sometimes a slight fever and depression. Joints are usually not swollen, but up to 25% can have joint synovitis. Symptoms can begin unilaterally but generally progress to bilateral appearance. They can be worse in the morning or after extended periods of sitting or lying down and can begin quickly or gradually. The disease can remit within 1 to 2 years without therapy. About 50% of patients will have a relapse after initial treatment.

GCA (also known as temporal arteritis) can occur alone or present with PMR (up to 60% of patients), whereas only 16% to 21% of patients with PMR have concomitant GCA. Symptoms include new headache, which is usually severe and near the temples, fever, anorexia, weight loss, depression, tender scalp, pain with chewing, jaw discomfort, tongue pain, loss of taste, and visual change. Patients with GCA can also experience swollen, inflamed, and red temple, neck, or arm arteries. Blindness sometimes occurs and is a medical emergency.
Besides physical examination, a shoulder and hip ultrasound to document bursitis or synovitis and some laboratory tests to document an inflammatory process will be helpful to rule in PMR and rule out other conditions. In PMR patients, generally the ESR (>30–50 mm/hr), platelet count, and C-reactive protein (>6 mg/dL) will be elevated; hemoglobin will be decreased with a mild, normochromic, normocytic anemia; and the rheumatoid factor will be negative. Sometimes a MRI or positron emission tomography scan are obtained. The ESR is elevated in GCA also. A temporal artery biopsy will be obtained to confirm GCA.

**Key Point:** The symptoms for polyarthralgia rheumatica and GCA are similar to other disorders, making diagnosis difficult.

**Summary of Standard Treatment and Review of Evidence Base Supporting Treatment Recommendations for Older Adults**

Because these conditions occur mostly in older adults, very few differences exist for treatment of older adults versus middle-aged adults. Glucocorticoids are considered first-line therapy for PMR because NSAIDs are usually inadequate. The starting prednisone dose is 15–20 mg daily for 2–4 weeks. In the past, quick response to glucocorticoids was a hallmark of PMR diagnosis, but newer data documented that up to 4 weeks can be required for complete response, which is achieved in only 70% of patients. During treatment initiation, the ESR should return to baseline, and if it does not, a different disease diagnosis should be considered. After 2–4 weeks, the oral glucocorticoids are then tapered. One tapering method is to decrease the daily dose by 2.5 mg every 2–4 weeks until 10-mg daily dose. This 10-mg dose is used for 1 month and then the daily dose is decreased by 1 mg every month until discontinuation or flare-up. Some prescribers use a slower taper, decreasing the dose over longer durations; thus, treatment can last for 1–2 years. Sometimes symptoms reappear, requiring extended duration of treatment. Methylprednisolone 120 mg intramuscularly every 3–4 weeks can be used, tapered by 20 mg every 2–3 months. Methotrexate, a steroid-sparing agent, is sometimes added in the attempt to decrease the long-term steroid dose and improve response; however, the data were mixed, and one study showed positive short-term effects but no difference in long-term benefits. Subsequent flares can be treated with the prednisone dose that initially controlled the disease with or without methotrexate added. Other immune-modulating medications are being explored but not recommended as first-line therapy.

The glucocorticoid therapy for GCA is higher (40–60 mg prednisone per day; about 0.7–1 mg/kg) than PMR, and it is preferably started after the biopsy but should not be delayed if biopsy is scheduled for a couple days later. Response should be seen within 24–72 hours. Similar to PMR, after 2–4 weeks of symptom remission, a slow taper is begun; about 10% decrease every 2–3 weeks until 10 mg daily followed by decreasing the dose 1 mg per day each month until discontinuation, which is usually 18–24 months after initiation. Methotrexate does not have a rapid onset of action but is effective for this condition. Therefore, this medication is generally reserved for relapses or patients with significant glucocorticoid adverse effects. TNFα inhibitors might be used in long-standing refractory GCA cases. Mixed results exist for the inclusion of low-dose aspirin to prevent GCA complications.

**Common Problems Encountered When Treating Older Adults with This Condition**

Glucocorticoids are associated with many adverse effects experienced by 65% to 81% of those with PMR and 25% to 50% (serious effects) of those with GCA. They can cause osteoporosis (as discussed), myopathies, and hypogonadism. Glucocorticoids can also cause, hasten progression, or worsen other comor-
bidities such as diabetes, cataracts, glaucoma, hypertension, and infection in some older adults, frequently requiring initiation or dose adjustment of medications for these conditions. They are associated with wasting/weakening of muscles, ligaments, tendons, and skin; drug-induced Cushing syndrome; and peptic ulcers. Many psychological adverse effects exist with these medications, with some of the medication-induced negative mood and behavior therapies compounding underlying depression and potential behavior problems in patients with Alzheimer disease. Glucocorticoids can increase GI bleeding risk secondary to medication-related peptic ulcer formation. Concomitant NSAIDs can further compound this risk. If long-term glucocorticoid use is warranted and prescribed with concomitant NSAIDs, a PPI might reduce GI bleeding risk. Ensuring older adult vaccinations are up to date is good practice before or early during long-term glucocorticoid therapy. Careful monitoring of an older adult is required to identify and resolve glucocorticoid-induced adverse effects.

**Pressure Ulcers**

*Etiology, Epidemiology, and Clinical Presentation Specific to Older Adults*

The older and more frail the patient, the higher the risk for pressure ulcer development. **Pressure, shear, and friction** are the three major factors in the formation of pressure ulcers. Patients older than 70 are at a greater risk for pressure ulcers. Additional factors, some of which have a higher prevalence in older adults, are found in Table 15-3. Critical care patients are at particularly high risk with a direct relationship with mechanical ventilation. The Braden scale and the Norton scale are two common scales used to predict pressure ulcer risk. Albumin is a laboratory parameter that can assist in the assessment of pressure ulcer risk, which needs to be adjusted for dehydration when interpreting results.

<table>
<thead>
<tr>
<th>Table 15-3. Factors Associated with Pressure Ulcers</th>
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<tbody>
<tr>
<td>Age over 70</td>
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<tr>
<td>Altered sensory perception</td>
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<tr>
<td>Altered mental state</td>
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<tr>
<td>Inability to perceive pressure</td>
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<tr>
<td>Comorbidities: diabetes, malignancy, stroke, heart failure, hypertension, renal failure, anemia, impaired circulation, urinary and fecal incontinence, lymphopenia</td>
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<tr>
<td>Infection (sepsis, fever, pneumonia)</td>
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<tr>
<td>Emergency department stay</td>
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<tr>
<td>Longer length of stay in a facility</td>
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<tr>
<td>Malnutrition (hypoalbuminemia)</td>
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<tr>
<td>Male gender</td>
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<tr>
<td>White or black race</td>
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<tr>
<td>Current smoking</td>
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<tr>
<td>Physical restraints</td>
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<tr>
<td>Dry and scaly skin or excessive skin moisture</td>
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<tr>
<td>History of pressure ulcers</td>
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<tr>
<td>Decreased activity level</td>
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<tr>
<td>Immobility or inability to reposition</td>
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<tr>
<td>Weight loss or low BMI</td>
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<tr>
<td>Surgical intervention</td>
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<td>Critical care, especially if receiving mechanical ventilation</td>
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**BMI, body mass index.**

Pressure ulcer prevalence is approximately 12% to 13%. The mean age of people with pressure ulcers is 72–73 years. The most common pressure ulcer sites are the heel, coccyx, and ear. Pressure ulcers are defined by stages indicating depth and severity. Stages range from I to IV, with additional categories for unstageable and suspected deep-tissue injury; see the National Pressure Ulcer Advisory Panel (NPUAP) website for pictures. Staging is based on the amount of tissue loss that has occurred, with stage IV representing full tissue loss to the point of bone, tendon, or muscle exposure.
Pressure ulcers have a significant impact on quality of life. Presence and treatment of pressure ulcers can lead to changes in environment such as a pressure-reduction bed, infringement on personal time, negative impact on sexual activity, loss of autonomy with function, and social isolation. Pressure ulcers are associated with pain, can lead to emotional difficulties including depression, have negative financial impact, and are associated with increased mortality.

**Summary of Standard Treatment**

Pressure ulcer care starts with prevention. The cost of treatment of a stage IV pressure ulcer far exceeds the cost of pressure ulcer prevention and early identification programs. Preventive techniques include avoiding or minimizing friction when changing positions, changing positions regularly, keeping skin clean and dry (proper incontinence care is particularly important), and avoiding vigorous massage (shear). For those patients that can, position shifts should occur at least every 15 minutes. For those patients who cannot, use of a mattress that redistributes weight is recommended with repositioning at least every 2 hours. Many available interventions, such as pressure-relieving boots, elevation of the head of the bed, foam supports with holes or indentations at boney prominences, and mattress overlays, are also available to decrease pressure on common pressure points (heels, coccyx, ischium, trochanter, shoulders, knees, ankles, and elbows) based on the contour of the human body. Good nutrition is another key to pressure ulcer prevention and wound healing. A balanced diet with supplements as needed is the minimum level of nutrition intervention required.

The 2009 NPUAP pressure ulcer guidelines can be used along with information from the 2008 guideline for pressure ulcers in long-term care. A protocol for the treatment of pressure ulcers can be found in Figure 15-2. This protocol involves steps to prevent, identify early, stage, monitor, treat, and resolve pressure ulcers. A multifactorial approach such as the one presented in Figure 15-2 plus treatment of concomitant conditions is essential for successful pressure ulcer resolution. Treatment involves debridement, cleansing, and dressing of the wound. Management of bacterial load is another important element. This should be done with debridement whenever possible, but antibiotics can be considered when debridement alone is not effective.

Wound debridement can be done in several different ways depending on the nature of the wound. For quick debridement, surgical (also known as sharp) debridement is typically used. Wet to dry debridement can be effective but does not differentiate healthy from unhealthy tissue well, so use has declined. Enzymatic debridement targets and digests the extracellular proteins in the unhealthy tissue.

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would ensure the patient can move to relieve pressure, if physically able. Oversedation can further increase pressure ulcer risk.\textsuperscript{124}

Appropriate antibiotic use is a key component of pressure ulcer healing. Systemic antibiotics are appropriate if clinical signs of infection exist, such as elevated fever, elevated white blood cell count, or red and swollen surrounding tissue.\textsuperscript{139} However, routine cultures of the wound bed do not yield useful results in directing antibiotic selection. Topical antibiotics are usually not recommended, with the possible exception of superficial infections.\textsuperscript{138} For deep tissue infections, including osteomyelitis, intravenous systemic antibiotics are required.

The seriousness of pressure ulcers and the need to prevent, identify early, and treat effectively are emphasized by many leading healthcare agencies. The Institute for Health Care Improvement, Centers for Medicare & Medicaid Services (CMS), the NPUAP, and the Surgeon General’s Healthy People 2020 are a few. The National Quality Forum with CMS has designated stage III and IV ulcers acquired in the hospital as “never errors,” which are serious and expensive medical errors that should never occur.\textsuperscript{141} CMS will reduce or not pay for hospital stays due to these hospital-acquired ulcers.

**Common Problems Encountered When Treating Older Adults with This Condition**

Many people over 65 have accumulated comorbid conditions and other variables associated with increased pressure ulcer risk. Medi-
### Table 15-4. Modern Classes of Dressings

<table>
<thead>
<tr>
<th>Class</th>
<th>Description</th>
<th>Tissue Debridement</th>
<th>Infection</th>
<th>Moisture Balance</th>
<th>Indications/Contraindications</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Films/membranes</td>
<td>Semipermeable adhesive sheet; impermeable to water molecules and bacteria.</td>
<td>+</td>
<td>-</td>
<td>-</td>
<td>Moisture vapor transmission rate varies from film to film. Should not be used on draining or infected wounds. Create occlusive barrier against infection.</td>
</tr>
<tr>
<td>2. Nonadherent</td>
<td>Sheets of low adherence to tissue. Nonmedicated tulles.</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>Allow drainage to seep through pores to secondary dressings. Facilitate application of topical.</td>
</tr>
<tr>
<td>3. Hydrogels</td>
<td>Polymers with high water content. Available in gels, solid sheets, or impregnated gauze.</td>
<td>++</td>
<td>/+</td>
<td>++</td>
<td>Should not be used on draining wounds. Solid sheets should not be used on infected wounds.</td>
</tr>
<tr>
<td>4. Hydrocolloids</td>
<td>May contain gelatin, sodium carboxymethylcellulose, polysaccharides, and/or pectin; sheet dressings are occlusive with polyurethane film outer layer.</td>
<td>+++</td>
<td>/+</td>
<td>++</td>
<td>Should be used with care on fragile skin. Should stay in place for several days. Should not be used on heavily draining or infected wounds. Create occlusive barrier to protect the wound from outside contamination. Odor may accompany dressing change and should not be confused with infection.</td>
</tr>
<tr>
<td>5. Acrylics</td>
<td>Clear acrylic pad enclosed between two layers of transparent adhesive film.</td>
<td>+++</td>
<td>/+</td>
<td>++</td>
<td>Use on low- to moderately draining wounds where dressing may stay in place for extended time. May observe wound without changing.</td>
</tr>
<tr>
<td>6. Calcium alginates</td>
<td>Sheets or fibrous ropes of calcium sodium alginate (seaweed derivative); have hemostatic capabilities.</td>
<td>++</td>
<td>+</td>
<td>+++</td>
<td>Should not be used on dry wounds. Low tensile strength: avoid packing into narrow deep sinuses. Biodegradable.</td>
</tr>
<tr>
<td>7. Composite dressing</td>
<td>Multilayered, combination dressings to increase absorbency and autolysis.</td>
<td>+</td>
<td>-</td>
<td>+++</td>
<td>Use on wounds where dressings may stay in place for several days.</td>
</tr>
<tr>
<td>8. Foams</td>
<td>Nonadhesive or adhesive polyurethane foam; may have occlusive backing; sheets or cavity packing; some have fluid lock.</td>
<td>-</td>
<td>-</td>
<td>+++</td>
<td>Use on moderately to heavily draining wounds. Occlusive foams should not be used on heavily draining or infected wounds.</td>
</tr>
</tbody>
</table>
### Table 15-4. (cont’d)

<table>
<thead>
<tr>
<th>Class</th>
<th>Description</th>
<th>Tissue Debridement</th>
<th>Infection</th>
<th>Moisture Balance</th>
<th>Indications/Contraindications</th>
</tr>
</thead>
<tbody>
<tr>
<td>9. Charcoal</td>
<td>Contains odor-absorbing charcoal within product.</td>
<td>–</td>
<td>–</td>
<td>+</td>
<td>Some charcoal products are inactivated by moisture. Ensure dressing edges are sealed.</td>
</tr>
<tr>
<td>10. Hypertonic</td>
<td>Sheet, ribbon, or gel impregnated with sodium concentrate.</td>
<td>+</td>
<td>+</td>
<td>++</td>
<td>Gauze ribbon should not be used on dry wounds. May be painful on sensitive tissue. Gel may be used on dry wounds.</td>
</tr>
<tr>
<td>11. Hydrophilic fibers</td>
<td>Sheet or packing strip of sodium carboxymethylcellulose; converts to a solid gel when activated by moisture (fluid lock).</td>
<td>+</td>
<td>–</td>
<td>+++</td>
<td>Best for moderate amount of exudates. Should not be used on dry wounds. Low tensile strength: avoid packing into the narrow deep sinus.</td>
</tr>
<tr>
<td>12. Antimicrobials</td>
<td>Silver, iodides, PHMB, honey aniline dyes with vehicle for delivery: sheets, gels, alginates, foams, or paste.</td>
<td>+</td>
<td>+++</td>
<td>+</td>
<td>Broad spectrum against bacteria. Should not be used on patients with known hypersensitivities to any product components.</td>
</tr>
<tr>
<td>13. Other devices</td>
<td>Negative-pressure wound therapy applies localized negative pressure to the surface and margins of wound.</td>
<td>–</td>
<td>+</td>
<td>+++</td>
<td>This negative pressure—distributing dressing actively removes fluid from wound and promotes wound edge approximation. Advanced skill required for patient selection for this therapy.</td>
</tr>
<tr>
<td>14. Biologics</td>
<td>Living human fibroblasts provided in sheets at ambient or frozen temperature; extracellular matrix. Collagen-containing preparations; hyaluronic acid, platelet-derived growth factor.</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>Should not be used on wounds with infection, sinus tracts, or excessive exudate or on patients known to have hypersensitivity to any of the product components. Cultural issues related to source. Advanced skill required for patient selection for this therapy.</td>
</tr>
</tbody>
</table>

PHMB, polyhexamethylene biguanide.

*Use with caution if critical colonization is suspected.

- no activity
  + minimal activity
  ++ moderate activity
  +++ strong activity

cations can also decrease mobility, alter perfusion, alter sensation, or negatively impact wound healing. Specific medication classes to avoid or at least carefully monitor in patients with high pressure ulcer risk include glucocorticoids, sedative/hypnotics, opioids, antipsychotics, tricyclic antidepressants, and antihypertensives.

Prevention, identification, and treatment of pressure ulcers have always been a challenge, especially when caring for frail older adults. The prevalence of pressure ulcers in a healthcare environment is an indicator of care quality. Those who audit or pay for care scrutinize both the frequency of pressure ulcer development as well as the effectiveness of wound healing programs. Pressure ulcer treatment requires addressing all of the many factors associated with risks, response to care, and caregiver and provider issues. This frequently requires interdisciplinary teams. Pharmacist participation on such teams has been demonstrated to contribute to improved patient outcomes.¹²³

**KEY POINT:** Because prevention is the first step to pressure ulcer treatment planning, patients should be immediately assessed on institutional placement or ambulation change of any kind.

Nutritional status and skin checks are both essential components of the prevention or treatment plan.
CASE 1: REHABILITATION UNIT OF A SKILLED NURSING FACILITY

Subjective:
BN is a 70-year-old widowed Asian American man in the rehabilitation program after sustaining a hip fracture of the femur neck followed by arthroplasty 2 weeks ago. His postsurgical pain is much improved.

Past Medical History:
Hypothyroidism, incontinence.

Medications:
Levothyroxine 100 mcg daily, tolterodine LA 2 mg daily, fondaparinux 2.5 mg daily (for total of 35 days then switch to warfarin for 5 months), aspirin 81 mg daily, Tylenol #3 1–3 per day prn (no longer using), and calcium chew with vitamin K1 twice a day prn.

Allergies:
NKDA.

Social History:
Quit smoking 10 years ago and has a beer a day; Meals on Wheels at home; diet low in dairy products; minimal exercise. Prior to hip fracture he lived independently in his own home. Wife died 3 years ago; two children with families residing nearby.

Family History:
Mother died age 68 years due to breast cancer; she had a hip fracture at 65 years old; father died age 83 years from a myocardial infarct; he had OA and dyslipidemia. BN has two sisters with osteoporosis.

Objective:
Ht 5’6” per stadiometer (past height 5’9”), Wt 160 lb, BP 160/95 mmHg, P 80 BPM, T 98.6°F, RR 18 BPM.

Physical Examination:
ROM improving but still limited. Difficulties with gait and balance. All other aspects within normal limits.

Labs:
TSH 0.6 mIU/L (nl 0.4–10 mIU/L), T4 12.8 mcg/dL (nl 4.6–12 mcg/dL), Scr 1.4 mg/dL, BUN 25 mg/dL, 25 (OH) vitamin D 22 ng/mL, albumin 3.1 g/dL (nl 3.4–5.4 g/dL); all other lab values within normal limits. Procedures: lunar DXA spine T-score –2.3, nonsurgical hip/femoral neck T-score –2.8, total hip T-score –2.5.

Assessment:
BN is a 70-year-old man doing well in physical therapy for postfracture rehabilitation. A walker is needed for mobility. He is at increased risk for a pressure ulcer due to poor nutrition prior to fracture. He has previously undiagnosed osteoporosis and vitamin D insufficiency.

Plan:
1. Begin alendronate 10 mg weekly; provide patient education using the teach-back method, and recheck for understanding in a week and on discharge to home.
2. Until warfarin therapy is completed, switch the calcium chew to calcium carbonate 1,250 mg with vitamin D 400 units once daily with food. Increase dairy (after determining no lactose intolerance) and other high calcium content food intake. Provide patient with
list of high calcium–containing foods. Educate patient on counting calcium intake from foods to try to achieve a daily calcium intake of 1,000 mg in divided servings, preferably from foods and beverages and, if needed, supplements.

3. Begin ergocalciferol 50,000 units weekly for 6 weeks, then begin vitamin D supplement 1,000 units daily. Reassess 25 (OH) vitamin D level in 4 months and adjust daily supplementation as needed.

4. Decrease levothyroxine dose to 88 mcg daily and reassess TSH in 4–6 months with additional decreases to achieve a TSH concentration in the middle of the normal therapeutic range.

5. Provide patient and caregiver with fall prevention guidelines and a checklist for home safety. If patient or caregiver cannot do this assessment, schedule a home visit by an occupational therapist.

6. Assess patient’s skin for hot spots (i.e., red spots from pressure but without skin breakdown) and pressure ulcers frequently.

**Rationale:**

1. BN has had a fragility fracture that warrants osteoporosis treatment, which has been found to be cost effective. He has also lost 3 inches in height. Based on NOF guidelines, the patient’s femoral neck DXA score prior to fracture would have warranted osteoporosis prevention therapy. According to guidelines, alendronate, risedronate, zoledronic acid, and denosumab are medications of choice. His estimated Cockcroft-Gault creatinine clearance is above 35 mL/min. Because he has no underlying renal pathophysiology besides aging, bisphosphonates are safe to use. Most Medicare Part D plans will require generic bisphosphonate therapy first with zoledronic acid and denosumab requiring prior authorization. More recent studies do not find a difference in adherence between weekly and monthly therapies. He (and caregiver) will require alendronate education, making sure directions are followed and the medication is not taken with other medications, especially calcium. Repeated reinforcement and education can help ensure proper bisphosphonate administration and medication safety, adherence, and persistence.

2. In this scenario, FRAX calculations are not necessary to determine osteoporosis medication need but can be helpful with patient education and motivation to practitioners to prescribe treatment and for BN to take his osteoporosis medications. His age, race, height, and his mother’s and his own hip fracture are his risk factors.

3. Patient has poor nutrition and osteoporosis; thus, he needs to improve his nutrition and increase his daily calcium and vitamin D intake to prevent further bone loss and future fractures. Improved nutrition will also help prevent pressure ulcers. If the calcium chew contains vitamin K, it can be problematic with warfarin, especially if used erratically, but is not a problem with injectable anticoagulants. A dietitian can determine BN’s nutritional needs and suggest a balanced diet. His daily calcium intake needs to be determined to make sure over calcium supplementation and risk of myocardial infarct do not occur. Calcium foods are preferred but if insufficient to meet adequate intakes, a calcium supplement can be used.

4. His vitamin D concentration is considered insufficient but not deficient. His replacement schedule should replenish his stores and then the NOF vitamin D recommendations of 800–1,000 units daily can be implemented. Alternatively, a higher daily dose, for example 4,000 units per day, could be used. Because biologic feedback and equilibrium of vitamin D takes some time, follow-up monitoring is usually done 3–6 months after replenishment and stabilization with a maintenance dose. His follow-up vitamin D assessment should be done at the same laboratory as the first assessment if the vitamin D assays have not been standardized.
5. Excessive levothyroxine replacement can increase bone metabolism. Currently BN’s TSH concentration is at the lower end of the normal range and his T4 is slightly higher than the upper limit of the normal range, suggesting excessive replacement and warranting a lower levothyroxine dose. Because the new equilibrium can take time, follow-up TSH monitoring is also done 3–6 months after a dosage change.

6. BN has osteoporosis and will benefit from a safe home environment, decreasing the likelihood of falls, which can be achieved by completing the home safety ideas for falls prevention as described in the above suggested websites.

7. Male gender, decreased mobility, advanced age, poor nutrition, and surgical intervention increase BN’s risk for a pressure ulcer, which can be prevented with modifications of risk factors, good nutrition, and mobility.

Case Summary:
Osteoporosis is common in older adults, and a proactive approach to preventing bone loss and preventing falls is required. Although men are at lower risk, as seen with BN, they still develop osteoporosis and fractures. Men also have higher mortality after an osteoporotic fracture, so close monitoring of BN is required. Nutrition is a common problem, especially for older adults who live alone. Pharmacologic interventions exist to improve BN’s quality of life and potentially extend life duration.
**Case 2: Interprofessional Geriatric Clinic**

**Subjective:**
SB is a 79-year-old African American woman living in an assisted living facility for the last 2 years since the death of her husband. For the past 4 weeks, she has experienced significant increase in joint stiffness lasting about 1 hour every morning, weakness, and fatigue.

**Past Medical History:**
RA for past 22 years with acceptable control over the past few years, gout with last attack 3 years ago, and hypertension.

**Medications:**
Methotrexate 7.5 mg weekly, etanercept 50-mg injection weekly, celecoxib 100 mg twice daily, and enalapril 10 mg daily. Occasional chewable calcium tablets. Previous treatments with various combinations of DMARD medications. Past glucocorticoid therapy for RA flares has been limited to 2–4 weeks of therapy with doses ranging from 5 to 10 mg per day.

**Allergies:**
NKDA.

**Social History:**
Negative for tobacco and alcohol use. SB has two children and five grandchildren living in other states. She worked for 28 years in a hosiery textile mill.

**Family History:**
Mother died age 61 years after 30 years with RA; father died age 82 years from a motor vehicle accident.

**Objective:**
Ht 5’3˝, Tt 173 lb, BP 156/76 mmHg, P 82 BPM, T 98.6 °F, RR 16 BPM. Pain today 8/10; average 1 month ago 4/10.

**Physical Examination:**
Joint and muscle aches in neck, shoulders, and hips significantly worse in the past 2 days. Patient also describes weakness and lethargy. Negative for synovitis.

**Labs:**
ESR 89 mm/hr (nl 0–30 mm/hr).

**Assessment:**
SB is a 79-year-old woman with suspected PMR in addition to longstanding RA.

**Plan:**
1. Initiate glucocorticoid therapy with prednisone 20 mg daily for 2 weeks then return to clinic. After 2 weeks, if symptoms are eliminated and the ESR has returned to normal, the prednisone can be tapered by 2.5 mg every 2–4 weeks. If symptoms persist, wait a month and then re-evaluate, and if symptoms decreased can try tapering again. If pain returns while tapering, return to previous dose that controlled symptoms, wait 2–4 weeks, then slow the taper schedule. Once the dose is at 10 mg, maintain for a week and try decreasing dose by 1 mg every month. Patient might require low-dose long-term (i.e., 1–2 years) prednisone therapy to eliminate pain and prevent symptom reoccurrence. Assess bone density to determine baseline before using long-term (>3 months) prednisone. As an African American woman, SB’s FRAX 10-year osteoporosis fracture risk score is 11% prior to glucocorticoids and 17% on glucocorticoids, giving her medium risk for glucocorticoid-induced osteoporosis, which warrants treatment. Her FRAX might underestimate her risk.
because it does not account for fracture risk from falls, which she experiences. She can be started on alendronate, risedronate, or zoledronic acid. Her daily calcium intake needs to be determined, or use the average for her age, approximately 600–640 mg of elemental calcium daily. Because glucocorticoids decrease calcium absorption, adequate intakes are higher (1,200–1,500 mg). She should be educated to increase the calcium in her diet but if not, supplements can be used. If she will be on a PPI, calcium citrate, which has acid independent absorption, can be used, or she should take the calcium carbonate with the evening meal. She should take 800–1,000 units of vitamin D daily from a vitamin D supplement or multivitamin.

2. Monitor blood pressure during glucocorticoid therapy and adjust enalapril if blood pressure exceeds 150/90 mmHg or if any symptoms of end-stage organ impact (e.g., extreme headache, chest pain, altered urine output).

3. Obtain patient’s tolerable pain level and use this as therapeutic goal until PMR controlled.

4. Monitor GI symptoms. Another option would be to start a PPI in conjunction with the glucocorticoid regimen, especially because the patient is also on a COX-2 inhibitor.

**Rationale:**

1. Glucocorticoids are the gold standard treatment for PMR. They have the additional benefit of assisting in confirmation of diagnosis. If a patient’s symptoms, and ESR and anemia, if present, respond to the therapy, then it is likely the patient has PMR. If this patient also had headache, jaw pain, and inflamed arteries in the temples, neck, and arms then GCA could also be considered. Higher glucocorticoid doses are used to treat GCA.

2. Symptom relief is the primary goal of therapy, but the long-term effects of glucocorticoid therapy will have to be managed. Glucocorticoids can decrease bone density and increase blood pressure, so it is important to evaluate this patient for osteoporosis and the need for antiresorptive therapy, monitor blood pressure, and adjust hypertensive medication as needed. Other problems should be monitored, such as increase in blood glucose and infections.

3. Sometimes older adults cannot describe their pain or have different means of expressing pain, such as decreased eating and sleeping and increased aggression. In addition, increased function and quality of life are important goals. SB is already on celecoxib, so a change in NSAID is unlikely to control the PMR pain. The glucocorticoid therapy should help control pain and joint inflammation.

4. Because glucocorticoids and celecoxib can cause GI ulcers, a PPI might prevent GI adverse effects instead of treating them after the fact.

**Case Summary:**

The sudden increase in pain and stiffness with concomitant fatigue and weakness could indicate PMR. This patient’s RA has been fairly well controlled with her current regimen for over 2 years making a flare up less likely. The location of the specific pain is not indicative of a gout flare. PMR is usually responsive to glucocorticoid treatment, and a good response to therapy helps to confirm the diagnosis. Glucocorticoids have many side effects that should be monitored, such as blood pressure changes, antihypertensive medication doses, and bone loss, which is highly likely in older adults, especially those with RA.
Fundamentals of Geriatric Pharmacotherapy

Chapter Summary

Musculoskeletal conditions have increased prevalence with increased age. Such conditions have a direct negative impact on function and increase fall potential. Through risk factor modification, exercise, healthy nutrition, and good medical care, some of these conditions can be prevented or onset delayed. The care of patients with these conditions requires a patient-specific approach taking into consideration all risk factors, concomitant medical conditions and medications, and patient preferences, tolerances, and longevity. The cornerstone of therapy for the musculoskeletal conditions covered is nonpharmacologic therapies. Pharmacologic therapy is one aspect of this care but carries associated risks and generally does not eradicate the disease. The medications commonly used to treat these conditions have adverse effect profiles that can further negatively impact function and comorbidities as well as increase morbidity. Some of these therapies require age-related adjustments. To maximize effectiveness and minimize risk, a healthcare professional with expertise in pharmacologic therapy is an important part of the healthcare team. Achieving and maintaining control of these conditions are keys for patient function, quality of life, and safety.

Self-Assessment Questions

1. What risk factors for musculoskeletal disease can be modified to prevent disease development?
2. What aspects of daily life could be modified to decrease the development or progression of musculoskeletal diseases?

3. How can you prevent falls, especially related to medication therapies?

4. What information is needed to calculate osteoporotic fracture risks for the FRAX estimation for an older adult?

5. Which medications for musculoskeletal disorders require dose adjustments due to age-induced decreases in renal or hepatic function?

6. Which medications for musculoskeletal disorders require attention to product selection based on comorbidities?

7. What are the risks of NSAIDs and COX-2 inhibitors in older adults, and how can you minimize these?

8. What patient comorbidities can be worsened with glucocorticoid therapy?

References


Learning Objectives

1. Characterize the common causes and complications of anemia and their prevalence in the elderly patient.
2. Develop a treatment plan for a patient with anemia that includes pharmacologic and nonpharmacologic therapy.
3. Summarize the current recommendations on immunization for older adults.
4. Given a patient case, recommend appropriate immunizations and monitoring parameters.
5. Describe various cancer screening tests that are recommended for the geriatric population, including associated problems and barriers.
6. Describe various cancer prevention measures, including medications and vitamin supplements.

Key Terms and Definitions

Cancer Chemoprevention: Use of natural, synthetic, or biologic chemical agents to reverse, suppress, or prevent carcinogenic progression to invasive cancer.

Erythropoiesis: The process of producing red blood cells.

Erythropoietin: Protein secreted by the kidneys that stimulates the production of red blood cells.

Ferritin: Main intracellular iron storage protein in the body.

Hematopoietic: Relating to the formation and maturation of blood cells and their derivatives.

Hepcidin: Hormone produced by the liver that regulates iron hemostasis. Hepcidin inhibits ferroportin, a protein found on enterocytes and macrophages that transports iron out of storage cells. Inhibition of ferroportin prevents iron release from macrophages as well as secretion of iron from the intestines into the hepatic portal system, thereby reducing iron absorption.
Fundamentals of Geriatric Pharmacotherapy

HUMORAL: Relating to the fluids of the body.

INTRINSIC FACTOR: Protein produced by the stomach that is necessary for the absorption of vitamin B12 in the terminal ileum.

MYELODYSPLASIA: Condition characterized by dysfunctional production of cells in the bone marrow and, thereby, ineffective hematopoiesis.

TRANSFERRIN: Plasma protein that binds to and transports iron in the body.

Introduction

Diseases of the hematologic and immune systems are common in the older adult. In addition, system decline theories of aging focus on failures with these systems as potential explanations for the frailty seen in many of the very old population. Anemia, cancer, and loss of immune function are common with aging but have yet to be identified as normal diseases associated with the aging process. Causes of anemia in the elderly patient and its proper treatment are reviewed in the first section of this chapter, followed by a section on immunizations. The chapter ends with a focus on cancer screenings appropriate for older adults. The tenets of public health provide the necessary prevention of infections and early detection of cancer that will aid older adults to live healthier, longer lives.

Anemia

Prevalence, Pathogenesis, and Etiology of Anemia Specific to Geriatrics

Prevalence

Anemia in the elderly has been termed a public health crisis due to its high prevalence and possibility for adverse consequences.1 As with many chronic diseases, the prevalence of anemia increases with increasing age.2 The Third National Health and Nutrition Examination Survey (NHANES III) of 2.8 million elderly patients with anemia documented an anemia prevalence rate of 10.6% in community-dwelling adults age 65 years or older, with prevalence rates increasing to 20% in women and 26% in men aged 85 years and older.2,3 Other reports have described substantially higher rates of anemia in the homebound elderly (39.6%) and in nursing home residents (48% to 63%).4-7

With regard to sex, there is a crossover in which anemia is more common in females less than 65 years of age but is more common in males over 75 years of age.2,3 This may be due to the sex-specific definition of anemia used by the World Health Organization (WHO), of a hemoglobin concentration of <13 g/dL in men and <12 g/dL in women.8 Although this distinction in defining anemia may be reasonable premenopause, some have questioned whether this is appropriate for postmenopausal females.2 If anemia is defined as a hemoglobin concentration of <13 g/dL regardless of sex, then the rates of anemia in women would appear to be higher than men regardless of age.2,9 Some have also questioned the value of using these hemoglobin thresholds so widely for diagnosing anemia, as the WHO criteria were developed for patients with nutritional anemia without the intent of becoming a diagnostic standard for all types of anemia.10 Also, as discussed later in this chapter, these hemoglobin cutoffs do not necessarily represent therapeutic goals nor thresholds at which to begin treatment. Racial differences have also been demonstrated with regard to anemia prevalence in the elderly, with a remarkably higher rate seen in African American individuals (Figure 16-1).2,3 The racial differences in hemoglobin concentration between African Americans and non-Hispanic Caucasians is believed to be due to genetic mutations that have evolved secondary to environmental pressures in Africa.
and Europe rather than due to health, nutrition, or behavioral or socioeconomic factors. Some have therefore advocated for racial distinctions in defining anemia, which is further supported by recent data demonstrating that a hemoglobin concentration below the current WHO threshold for anemia is associated with increased mortality in African American patients.

Pathogenesis and Etiology

The fundamental cause of most anemia in elderly patients is defective or deficient red blood cell production, otherwise known as diminished erythropoiesis. Age-related changes in erythropoiesis may be considered in the context of two broad categories: (1) changes intrinsic to erythroid progenitor or hematopoietic stem cells, and (2) changes in humoral control mechanisms. With regard to alterations in progenitor and stem cells, morphologic studies have shown a decrease in hematopoietic tissue in the bone marrow of elderly patients, although erythropoietic activity is not necessarily diminished. Whereas some studies have shown a decrease in erythroid burst-forming and colony-forming units in anemic elderly patients, other studies have shown no changes. One study in particular showed a lower number of CD34+ progenitor cells in the blood of elderly (but not necessarily anemic) individuals with an increase in serum stem cell factor concentrations, which may be a compensatory mechanism to stimulate erythroid cell differentiation. In this study, CD34+ cells, in the presence of optimal concentrations of recombinant hematopoietic growth factors, were able to form erythroid burst-forming units and colony-forming units at a rate similar to that seen in young individuals. This would indicate that humoral mechanisms may be more likely responsible for the hematopoietic changes seen in the elderly as opposed to an unresponsiveness of hematopoietic progenitors to growth factors.

From a humoral perspective, erythropoietin concentrations generally increase with aging, although studies have shown mixed results in this

Figure 16-1. Prevalence of anemia in individuals aged 65 or older in the United States by self-declared racial or ethnic group.
Source: Data from references 2 and 3.
Confounding this issue is that worsening renal function, which is often present in the elderly, corresponds to a blunted erythropoietin response to anemia and lower erythropoietin concentrations. It has been theorized that the increase in erythropoietin concentrations seen with aging is a consequence of a state of relative erythroid resistance to erythropoietin, thereby resulting in increased erythropoietin secretion. Anemia then develops when this feedback loop is interrupted, which may occur in the presence of renal disease, diabetes, or hypertension.

Other humoral links to anemia have been made with testosterone, growth hormone, and inflammatory mediators. The androgenic hormones may play a role in erythropoiesis and their secretion decreases with aging. Associations have been made with low testosterone concentrations and anemia and, independently, growth hormone administration has been shown to reverse anemia in adults with growth hormone deficiency. However, direct links between androgen hormone deficiency and the development of anemia are lacking and require further study. Conversely, concentrations of inflammatory mediators are known to be chronically, albeit mildly, elevated in elderly individuals even in the absence of an acute illness or autoimmune disease. Concentrations of interleukin (IL)-6, IL-1β, tumor-necrosis factor (TNF)-α, C-reactive protein (CRP), and macrophage migration inhibitory factor (MIF) have been shown to be elevated in elderly patients with anemia compared to nonanemic counterparts, although compared with other types of anemia, inflammatory markers do not seem to be elevated in patients with anemia of unexplained etiology. In addition, elevated cytokine concentrations may impede erythropoietin production and impair erythropoiesis. Specifically, MIF and TNF-α interfere with erythroid colony formation and IL-6 and IL-1 increase hepatic synthesis of hepcidin, a polypeptide that inhibits both iron absorption from the gut as well as the release of iron from bone marrow macrophages to erythroid progenitors. Anemia in the elderly, especially anemia of inflammation, has also been associated with vitamin D deficiency, presumably due to the abilities of vitamin D to suppress inflammatory pathways and to regulate iron homeostasis by suppressing hepcidin.

The major causes of anemia in the elderly can be divided into four general categories: (1) iron-deficiency anemia, (2) nutrient-deficiency anemia (folate and/or vitamin B12), (3) anemia of chronic inflammation/kidney disease, and (4) unexplained anemia. Studies have documented the following regarding prevalence of anemia in the elderly: iron-deficiency anemia 12% to 25%, nutrient-deficiency anemia 1% to 18%, and anemia of chronic inflammation/kidney disease 10% to 32%. The most common etiology in these studies was unexplained anemia, occurring at a prevalence of 34% to 44%. Sometimes and perhaps inaccurately included in the category of unexplained anemia is anemia due to hematologic malignancy, the prevalence of which has been documented at 8% to 22% of patients referred to a hematology clinic. Some categorizations include iron-deficiency anemia as a nutrient-deficiency anemia, although a nutritional deficiency of iron is usually not the cause of this anemia in the vast majority of patients. In developing countries, iron-deficiency anemia may in fact be related to a dietary deficiency of iron, but nutritional iron deficiency is rare in Western society and most cases of iron-deficiency anemia in this population are due to bleeding and should be evaluated with this in mind.

Regarding nutrient-deficiency anemia, NHANES III documented an 18% prevalence of folate and/or vitamin B12 deficiency in elderly patients with anemia. However, more recent studies have placed the prevalence of folate and vitamin B12 deficiency anemia at less than 1% in the elderly American population referred to specialty hematology clinics. However, these patients are likely representative of neither the general population nor of the population seen by a general practitioner. It is also believed that in 30% to 50% of elderly anemic patients, multiple etiologies are responsible. Most cases of anemia in the elderly are mild; about 90% of patients have a hemoglobin of 11 g/dL or greater.
and about 98% have a hemoglobin of 10 g/dL or greater.2

Iron-Deficiency Anemia

Iron-deficiency anemia is usually due to bleeding, typically from the gastrointestinal tract, either from gastritis, ulcer disease, arteriovenous malformations, colon polyps, colorectal cancer, or hemorrhoids. If blood loss cannot be detected, then disorders involving iron absorption and bioavailability should be considered. In the elderly, atrophic gastritis may reduce iron absorption, and this condition is present in 20% to 48% of the elderly.38-41 Although the gold standard for diagnosing iron-deficiency anemia is the absence of iron on a stained bone marrow aspirate sample (rarely done) or an unambiguous hemoglobin response to a trial of iron,37 a clinical diagnosis is typically made by a standard blood test that demonstrates low serum iron and ferritin concentrations and a high total iron binding capacity (TIBC). However, in the elderly this is complicated by the fact that serum ferritin concentrations rise with advancing age, probably as a consequence of low-grade inflammatory processes.39 Consequently, serum ferritin concentrations below 45 mcg/L are usually indicative of iron deficiency in the elderly, whereas much lower concentrations may define iron deficiency in younger individuals.39,42 Measuring serum transferrin receptor (sTfr) concentrations has been proposed as a more sensitive estimate of iron stores in the elderly, but the lack of standardized reagents for this assay have obstructed the widespread use of this test in clinical practice.37,43

KEY POINT: Iron deficiency anemia is typically not due to poor dietary iron intake but a result of blood loss, most often from the gastrointestinal tract.

Vitamin B12- and Folate-Deficiency Anemia

Although vitamin B12 deficiency may result from dietary deficiency or a complication of gastrointestinal surgery, the most common cause worldwide is pernicious anemia, accounting for 76% of cases of vitamin B12-deficiency anemia.44,45 The median age range for pernicious anemia is 70–80 years, demonstrating a predilection for the elderly. A greater prevalence (about 4%) of pernicious anemia has also been documented in elderly persons of African or European ancestry compared to those of Asian ancestry.44 Pernicious anemia is an autoimmune gastritis characterized by the reduced ability of intrinsic factor to bind ingested vitamin B12 as a result of gastric parietal cell destruction.44 This leads to malabsorption of vitamin B12 that takes years to manifest. This is due to the relatively large body stores of vitamin B12 (about 2,500 mcg) in relation to the daily requirement (1 mcg). The recommended daily allowance of vitamin B12 of 2.4 mcg is to account for the incomplete ability of intrinsic factor to facilitate the absorption of vitamin B12. Individuals with pernicious anemia lack intrinsic factor and only absorb about 1.2% of ingested vitamin B12.45 Testing for pernicious anemia involves testing for anti-intrinsic factor or anti-parietal-cell antibodies.44 Although not as severe as pernicious anemia, up to 20% of the elderly may suffer from a milder form of atrophic gastritis with hypochlorhydria, which leads to an inability to efficiently release vitamin B12 from food, thereby resulting in mild malabsorption and a delayed and often subclinical manifestation of vitamin B12 deficiency.44,45

KEY POINT: Vitamin B12-deficiency anemia is the only nutritional anemia more prevalent among elderly and is usually caused by vitamin B12 malabsorption due to autoimmune gastritis.

Currently, folic acid fortification of dietary sources (especially flour) causes folate-deficiency anemia to be rare in all age groups. In fact, only 0.1% to 0.4% of folate tests ordered by providers demonstrate low folate concentrations.46,47 Compared to younger adults, older adults have been shown to have higher folate
concentrations both before and after the introduction of folic acid fortification.48,49

**Anemia of Inflammation and Anemia of Chronic Kidney Disease**

These types of anemia are sometimes grouped together under the broad heading of *anemia of chronic disease* because of the difficulty in establishing a clinical diagnosis; also, it is possible for them to occur together. *Anemia of inflammation* (a.k.a. anemia of chronic inflammation) has been described as a state of elevated inflammatory cytokines that stimulates the production of hepcidin in the liver, leading to a reduction in the intestinal absorption of iron and release of iron from macrophages. This manifests as low concentrations of serum iron in the presence of normal or increased total iron stores.2 The distinction of anemia of chronic inflammation and iron-deficiency anemia, therefore, is a diagnostic conundrum in the elderly, especially in the patient with a serum ferritin concentration in the intermediate range (e.g., 20–100 mcg/L), which can be seen with both types of anemia. Many epidemiologic studies are now defining anemia of inflammation as a serum iron <60 mg/dL along with a normal or elevated serum ferritin and the absence of other causes of anemia.37 As mentioned above, the sTfr index may be helpful in distinguishing these types of anemia, but is not widely used. Further complicating a diagnosis are the findings that: (1) inflammatory markers may normally increase with aging without necessarily being associated with anemia, (2) inflammatory markers may be elevated with anemia regardless of its etiology, and (3) inflammatory markers may not be markedly elevated with anemia of inflammation.37,50 The lack of standardized criteria for a diagnosis of anemia of inflammation helps to explain the difference in prevalence rates reported in the literature. NHANES III reported that 24% of all cases of anemia in the elderly are due to inflammation,2 but when stricter criteria are employed that base a diagnosis of anemia of inflammation on the presence of an active inflammatory condition such as infection, autoimmune disease, or malignancy, the prevalence drops to 6% to 10%.35,36

Anemia of chronic kidney disease is believed to be due to reduced erythropoietin production in the kidney, which is responsible for about 90% of the production of this hormone. In this setting, the kidney loses the ability to effectively produce erythropoietin in response to decreased oxygenation.51 In the elderly, anemia associated with chronic kidney disease represents 12.5% of all anemia cases,2 although estimates from specialty hematology clinics have been as low as 3% to 4%.35,36 In patients over 50, even mild degrees of renal insufficiency (creatinine clearance of 30–50 mL/min) are associated with anemia, and a direct association between degree of renal insufficiency and prevalence of anemia has been documented.52 The relationship of renal function, erythropoietin, and anemia in the elderly was investigated in the InCHIANTI study, which showed a progressive increase in anemia prevalence and a progressive decrease in renal function and hemoglobin with advancing age.53 A linear inverse relationship was seen with regard to anemia prevalence and kidney function (i.e., decreased kidney function = increased anemia prevalence), with creatinine clearances of 30 mL/min or lower.53 Inflammation may also contribute to anemia of chronic kidney disease, because high levels of inflammatory markers have been observed in these patients.50 A diagnosis of anemia of chronic kidney disease is made when chronic kidney disease is present and the hemoglobin concentration is <13.0 g/dL in males and <12.0 g/dL in females.54

**Unexplained Anemia**

The term *unexplained anemia* refers to anemia that has not been attributed to some other cause and is the most common anemia occurring in the elderly.2,35,36 It is believed that with an appropriate hematological evaluation many cases of unexplained anemia may be attributed to myelodysplasia.36,37 However, even with an intensive hematologic investigation, an underlying cause cannot be found in 35% to 44% of patients.35,36 Unexplained anemia is somewhat of a misnomer because this type of anemia is more likely due to the interplay of many different causes as opposed to ignorance of the cause. Although
some have coined unexplained anemia as a waste-basket diagnosis, it may actually be a distinct clinical entity with all cases sharing a unifying cause.\(^37\) Hormonal deficiency (e.g., low testosterone) and dysregulation of growth hormone/insulin-like growth factor-1 control of hepatic erythropoietin secretion have been proposed as possible causes of unexplained anemia.\(^37,55,56\) Unexplained anemia is usually mild, with hemoglobin concentrations about 1 g/dL lower than the standard set forth by the WHO, likely resulting in underdiagnosis.\(^57\) Age-related factors that contribute to unexplained anemia in the elderly are:

- renal dysfunction leading to a reduced response to erythropoietin,
- reduction in hematopoietic stem cell proliferative and regenerative function,
- lower androgen levels, resulting in a decline in hemoglobin concentration of up to 1 g/dL,
- chronic inflammation and cytokine dysregulation, and
- myelodysplasia.

Additionally, other comorbidities and medications as well as nutritional deficits and alcohol abuse may further contribute to the etiology of unexplained anemia. As most of these contributors are age-related, the prevalence of unexplained anemia is directly related to age, most common in the very old and virtually nonexistent in those less than 50 years of age.\(^57\)

**Summary of Standard Treatment in General Adult Population and Considerations in the Elderly**

**Iron-Deficiency Anemia**

The treatment of iron deficiency anemia involves iron supplementation to correct the anemia and replenish body stores.\(^58\) This can be done through diet in some cases but is usually achieved through iron supplements. Iron supplementation is typically via the oral route, but can also be given parenterally in patients with malabsorption or intolerance to oral preparations. Historically, in younger adults, iron-deficiency anemia was treated with a total oral daily dosage of 200 mg elemental iron, given in two or three divided doses. Lower dosages are recommended in the elderly patient to improve tolerability and reduce the risk of constipation, with the understanding that iron stores will replenish at a slower rate.\(^59,60\) More recent recommendations, however, favor lower daily dosages for all adult patients and recommend administering no more than 325 mg/day of iron sulfate (65 mg elemental iron).\(^61\) Daily dosages of elemental iron as low as 15 mg have been shown to be effective and well tolerated in the elderly, resulting in comparable increases in hemoglobin compared with 50-mg and 150-mg daily dosages, but with significantly lower rates of gastrointestinal adverse effects.\(^62\) In addition, a 20-mg daily dosage of elemental iron has been shown to be effective and safe in preventing iron deficiency anemia in pregnant women, supporting the use of low-dose iron therapy in the younger adult population.\(^63\) Preferably, iron should be administered at least 1 hour before meals because food will reduce iron absorption.\(^59\) However, gastrointestinal adverse effects may be minimized by taking iron products with food, necessitating this strategy in some patients. Because acid conditions improve iron absorption, the administration of ascorbic acid (250–500 mg twice daily) or orange juice with the iron preparation may be used, but its effectiveness in the treatment of iron-deficiency anemia is unknown.\(^58\)

Oral iron should be continued for 3 months after the iron deficiency has been corrected, to replenish body stores.\(^58\) Restoration of iron stores and subsequent improvement in hemoglobin may take about 4 months, with expected increases in hemoglobin of 1–2 g/dL every couple of weeks.\(^64\) Should oral iron therapy fail or not be tolerated, parenteral iron may be administered, although this form of therapy is more expensive and cumbersome to administer than oral therapy and possesses a risk of anaphylactic reactions. Although the initial rise in hemoglobin is more rapid with parenteral iron, the rise in hemoglobin at 12 weeks is similar to that seen with oral iron administration.\(^58\) Severe cases of
iron-deficiency anemia may necessitate red blood cell transfusion. When choosing a treatment plan for a patient with iron-deficiency anemia, the duration of therapy should not be longer than necessary, and a thorough risk-benefit analysis should be performed in any patient to determine whether high-dose oral therapy (i.e., greater than 65 mg elemental iron daily), parenteral iron therapy, or even red blood cell transfusion is really necessary given the higher risks of each of these treatments compared to low-dose oral iron supplementation. Overly aggressive therapy with iron products may result in high body stores of iron, which could lead to adverse clinical effects such as hemochromatosis, coronary artery disease, diabetes, Parkinson disease, and recurrent infections.

**Vitamin B12- and Folate-Deficiency Anemia**

In general, the treatment of anemia of nutritional etiology does not differ between elderly patients and younger adults. The treatment of vitamin B12 deficiency anemia is administration of exogenous vitamin B12. This can be obtained through food sources or more efficiently through high-dose oral or parenteral supplementation. High-dose oral and intramuscular administrations are equally effective. Oral vitamin B12 may be obtained without a prescription, and injections may be self-administered in many patients. Given that the majority of cases in the elderly are due to pernicious anemia, lifelong therapy is usually necessary and daily oral or monthly subcutaneous/intramuscular injections of 1 mg vitamin B12 are indicated. In these individuals, dietary fortification is usually an insufficient means of restoring vitamin B12 stores because of the malabsorptive nature of the condition. It has been recommended that individuals 50 years of age and older consume vitamin B12 in its crystalline form, which does not require gastric acid or enzymes for digestion. Patients with severe abnormalities should receive injections of 1 mg at least several times per week for 1–2 weeks, then weekly until improvement is shown, then monthly thereafter. With treatment, reticulocyte count increases in 1 week, with reversal of the anemia usually occurring in about 6–8 weeks.

**KEY POINT:** The treatment of anemia in adults differs little based on patient age, although considerations need to be made for the multiple comorbidities often occurring in the elderly.

Folate-deficiency anemia is treated with oral folic acid or, rarely, with parenteral folic acid. The dosage is typically 1 mg daily but may be as high as 5 mg daily in cases of malabsorption. Given the infrequency of this type of anemia, underlying causes should be considered prior to the initiation of folate therapy. Specifically, malabsorption and alcoholism, which interferes with folate absorption and metabolism, should be ruled out, and drug-induced causes should also be considered. Methotrexate, pentamidine, trimethoprim, and triamterene are folate antagonists. Azathioprine, 6-mercaptopurine, 5-fluorouracil, hydroxyurea, and reverse transcriptase inhibitors (e.g., stavudine, lamivudine, and zidovudine) may cause folate deficiency by directly inhibiting DNA synthesis. Cholestyramine, metformin, and sulfasalazine may decrease folate absorption. The anticonvulsants phenytoin, phenobarbital, primidone, and valproic acid may cause folate deficiency through impaired vitamin absorption and/or altered metabolism.

**Anemia of Chronic Kidney Disease, Anemia of Inflammation, and Unexplained Anemia**

Anemia of chronic kidney disease has been associated with reduced quality of life, increased cardiovascular risk, and possibly reduced survival. Treatment is therefore targeted at improving these outcomes and typically involves a combination of iron supplementation and erythropoietin-stimulating agents (ESAs). Oral iron therapy in this situation is often inadequate because of poor absorption, and parenteral therapy is often employed. Parenteral iron improves the response to ESAs and also provides a dose-sparing effect for these agents. The use of ESAs for treating chronic kidney disease is based on the need to stimu-
late erythropoiesis in a condition characterized by low production of this hormone. ESA therapy is considered when the hemoglobin is less than 10.0 g/dL but is not recommended if the hemoglobin concentration is 10.0 g/dL or higher. The Kidney Disease Improving Global Outcomes guidelines suggest that ESA therapy not be used to maintain hemoglobin concentrations above 11.5 g/dL, whereas the U.S. Food and Drug Administration (FDA) does not specify a hemoglobin target but rather recommends using the lowest dose of ESA sufficient to reduce the need for red blood cell transfusions. There are insufficient data with hemoglobin targets between 11.6 and 13.0 mg/dL, but this may be considered if the benefit of improved quality of life is deemed to exceed the risks of therapy. Hemoglobin concentrations should not exceed 13 g/dL in patients with chronic kidney disease who are receiving ESAs. These hemoglobin cutpoints were established in consideration of the risk-benefit ratios seen with ESA therapy in clinical trials. The potential for harm is believed to exceed the benefits when achieving higher hemoglobin concentrations with ESA therapy; the risks associated with higher hemoglobin targets are stroke, hypertension, vascular access thrombosis in dialysis patients, and possibly death. Epoetin-alfa (Epogen, Procrit), darbepoetin-alfa (Aranesp), and methoxy polyethylene glycol-epoetin beta (Mircera) are the ESAs approved in the United States for treating anemia of chronic kidney disease.

Anemia of inflammation and unexplained anemia are treatment challenges due to the multifactorial nature of these conditions. Identifying and treating the underlying causes is the logical approach, but most of these causes have limited treatment options themselves, and isolating each cause is a challenge in and of itself. Complicating matters is the lack of clinical trial data to help guide the decision-making process with regard to treatment. To begin, it is recommended to treat any identifiable cause that is amenable to treatment (e.g., nutritional deficiency). Should anemia persist, then ESA therapy may be considered. Two small studies in elderly patients with anemia of chronic disease have demonstrated the benefits of epoetin alfa for treating this condition. In these reports (n = 17, combined), mean hemoglobin increases of 3–4 g/dL were seen in the majority of patients.

**KEY POINT:** Anemia in the elderly has been repeatedly linked to a number of serious complications, even with mildly depressed hemoglobin concentrations.

**Common Problems Associated with Anemia in the Elderly Patient**

Anemia has been shown to be an independent predictor of mortality in elderly in both the community as well as the nursing home settings.

Anemia has also been associated with cognitive impairment in the elderly. One case-control study documented an association between anemia and a higher risk of being diagnosed with Alzheimer disease. Another longitudinal study showed an association between anemia and the subsequent diagnosis of dementia. Mild anemia (hemoglobin 10–12 g/dL) has also been linked with a reduction in executive function (a set of high-level cognitive abilities involving goal-oriented tasks) in elderly community-dwelling women. More recently, a systematic review documented a significant hazard ratio of 1.94 for the risk of incident dementia in the elderly with anemia. However, the low number of studies in this area allowed only two to be included in this analysis.

Physical function in the elderly is also adversely affected by anemia, even in its milder forms. The Women’s Health and Aging Study showed that even the mildest forms of anemia (i.e., hemoglobin concentrations of 12 g/dL) were associated with mobility difficulties compared with hemoglobin concentrations in the normal range. Frailty is also more likely with hemoglobin concentrations of 12 g/dL or lower compared with concentrations of 13.5 g/dL. Anemia in the elderly has also been associated...
with reduced muscle strength, an increased risk of falls, a decline in physical performance, an increased likelihood for hospitalizations, and an increased length of stay once hospitalized.\(^\text{87-93}\)

Although the overall goals of treating anemia in the elderly are to decrease the morbidity and mortality associated with this condition, it is difficult to judge success of treatment based on these parameters because of the presence of other comorbidities and a lack of clinical trial data that directly address this issue. Treatment success is, therefore, often based on other more achievable outcomes, such as alleviation of symptoms and an improvement of hematologic parameters. A diagnostic work-up of any anemia may lead to the identification of an underlying cause (e.g., bleeding) and, with proper treatment of that cause, the prevention of potentially serious consequences. Although treatment success for some types of anemia (e.g., iron deficiency, vitamin B12 deficiency) is judged to some extent based on a rise in hemoglobin concentration, the efficacy of pharmacologically correcting low hemoglobin concentrations to achieve a goal hemoglobin of 12–15 g/dL is largely unknown for preventing the long-term morbidities and mortality associated with anemia in the elderly. There is evidence of a J-curve phenomenon that shows elevated complication rates with hemoglobin concentrations of 11 and 12 g/dL and >15 g/dL, with lower complication rates in between these values.\(^\text{78,81}\) In fact, as discussed earlier, current recommendations for treating anemia of chronic kidney disease advise against pushing the hemoglobin concentration over 13 g/dL because of an unfavorable risk-benefit ratio.\(^\text{54,70,71}\) As such, the target hemoglobin concentration for treating anemias with pharmacologic intervention and the benefits of such intervention remain largely unknown.

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**Immunizations**

**Influenza**

Older patients experience several age-related changes in the immune system (discussed in Chapter 17) that increase vulnerability to infection. Epidemics of influenza are caused by influenza A (H1N1), influenza A (H3N2), and influenza B viruses. Influenza activity begins as early as October and may continue through May or even beyond in North America. Nationally in 2013–2014, more than 50% of all reported influenza hospitalization occurred in adults aged 65 and older.\(^\text{54}\) Vaccination is the most effective method to prevent the mortality and morbidity associated with influenza and its complications (pneumonia, secondary infection, exacerbations of chronic diseases, and death).\(^\text{55}\) Influenza vaccination resulted in an estimated 79,000 (17%) fewer hospitalizations during the 2012–2013 influenza season and prevented approximately 6.6 million influenza illnesses and 3.2 million medically attended illnesses.\(^\text{94}\) Each year at least one or more virus strains in the vaccine might be changed based on global surveillance of the emergence and spread of new strains. Traditional trivalent influenza vaccines protect against three strains of influenza virus. A new trivalent influenza vaccine manufactured using non-egg-based cell culture technology was approved for patients 18 years and older. Its shorter manufacturing time could be desirable in the event of a pandemic or vaccine supply shortage. However, it does contain a trace of egg protein and could still potentially cause reaction in people who have egg allergies. Another new quadrivalent vaccine contains antigen from both B strain lineages and may offer additional protection against influenza-related adverse outcomes.\(^\text{95}\)

The Advisory Committee on Immunization Practices (ACIP) recommends influenza vaccination early in October or November until the supply is exhausted.\(^\text{95}\) The primary target groups are persons with high risk for influenza complications, including all persons over 50 and younger persons with chronic medical conditions (see Table 16-1). Individuals who are in contact with the high-risk target groups should also be vaccinated to prevent transmission of infection. These include healthcare personnel; staff of long-term care facilities, assisted living, and other residential settings; household contacts; and caregivers of high-risk groups who are at risk for severe complications from influenza.\(^\text{95}\)
Table 16-1. Adult Target Groups for Influenza, Pneumococcal, and Herpes Zoster Vaccinations

<table>
<thead>
<tr>
<th>Vaccine</th>
<th>Adult Target Groups</th>
</tr>
</thead>
<tbody>
<tr>
<td>Herpes zoster</td>
<td>All adults aged ≥60 years with no contraindications to vaccines</td>
</tr>
<tr>
<td>Influenza</td>
<td>Adults age ≥50 years</td>
</tr>
<tr>
<td></td>
<td>Residents of nursing homes or other long-term care and assisted living facilities</td>
</tr>
<tr>
<td></td>
<td>Women who will be pregnant during the influenza season</td>
</tr>
<tr>
<td></td>
<td>Patients with chronic pulmonary diseases (including asthma); cardiovascular disorders (except hypertension); renal, hepatic, hematological, or metabolic disorders (including diabetes mellitus)</td>
</tr>
<tr>
<td></td>
<td>Persons who have immunosuppression, including that caused by medications or human immunodeficiency virus (HIV)</td>
</tr>
<tr>
<td></td>
<td>Persons who have any conditions that can compromise respiratory function (e.g., cognitive dysfunction, spinal cord injury, or seizure disorder or other neuromuscular disorders); or the handling of respiratory secretions that can increase the risk of aspiration</td>
</tr>
<tr>
<td></td>
<td>Health care personnel</td>
</tr>
<tr>
<td></td>
<td>Household contacts and caregivers of children aged &lt;5 years and adults age ≥50 years, with particular emphasis on vaccinating contacts of children age &lt;6 months</td>
</tr>
<tr>
<td></td>
<td>Household contacts and caregivers of persons with medical conditions that put them at high risk for severe complications from influenza</td>
</tr>
<tr>
<td>Pneumococcal</td>
<td>Age ≥65</td>
</tr>
<tr>
<td></td>
<td>Chronic pulmonary disease, excluding asthma</td>
</tr>
<tr>
<td></td>
<td>Chronic cardiovascular disease</td>
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<tr>
<td></td>
<td>Diabetes mellitus</td>
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<tr>
<td></td>
<td>Chronic liver disease, including cirrhosis due to alcohol abuse</td>
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<tr>
<td></td>
<td>Chronic alcoholism</td>
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<tr>
<td></td>
<td>Chronic renal failure or nephritic syndrome</td>
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<tr>
<td></td>
<td>Functional or anatomic asplenia (sickle cell disease or splenectomy)</td>
</tr>
<tr>
<td></td>
<td>Immunosuppressive conditions</td>
</tr>
<tr>
<td></td>
<td>Cochlear implants</td>
</tr>
<tr>
<td></td>
<td>Cerebrospinal fluid leaks</td>
</tr>
<tr>
<td></td>
<td>Alaska Natives and certain American Indian populations</td>
</tr>
<tr>
<td></td>
<td>Residents of nursing homes or other long-term care facilities</td>
</tr>
<tr>
<td>Tetanus, diphtheria,</td>
<td>Persons aged 11 years or older who have not received Tdap vaccine or for whom vaccine status is unknown should receive a dose of Tdap followed by Td booster every 10 years thereafter</td>
</tr>
<tr>
<td>acellular pertussis</td>
<td>Adults who have completed a primary series and the last vaccination was received ≥10 years previously</td>
</tr>
<tr>
<td>(Td/Tdap)</td>
<td>Wound management</td>
</tr>
</tbody>
</table>

In 2012–2013, vaccine effectiveness in preventing influenza-related outpatient medical visits was 52% overall, but with decreased effectiveness in adults aged 65 and older (32%). In 2011–2012, vaccinated adults aged 50 and older had a 77% lower risk of related hospitalization. A study suggests a savings of $980 per quality-adjusted life year with influenza vaccination among persons aged ≥65. Pharmacy-based vaccination programs have increased the senior influenza vaccination rate in New York City from 52% to 67% in 2009 and 2011, respectively.

Adults 50 years of age and older and their household contact/caregivers should receive an annual single dose of inactivated influenza vaccination (0.5 mL) intramuscularly in the deltoid muscle soon after vaccine becomes available, if possible by October. Adults age 65 and older may receive either standard or high-dose influenza vaccine. Intranasal live attenuated influenza vaccine is not indicated for this target group. Currently, there is no recommendation regarding using trivalent versus quadrivalent vaccine, but it is important to remember that the quadrivalent vaccine will provide additional protection only if the fourth strain of influenza actually circulates. Clinicians should immunize patients with any appropriate influenza vaccine that is available.

Influenza vaccination is contraindicated in persons with a previous severe allergic reaction to the vaccine or egg protein. The most common side effects are injection site soreness, redness, swelling, low-grade fever, aches, itching, and fatigue. Persons with moderate or severe acute illness should defer receiving the vaccine until symptoms subside. A history of Guillain-Barré syndrome within 6 weeks following a previous dose of inactivated vaccine is considered a precaution for its future use. Antiviral chemoprophylaxis is not a substitute for vaccination but is recommended for healthcare workers and people at higher risk for complications if vaccine is medically contraindicated. Oseltamivir (Tamiflu) capsules and zanamivir (Relenza) oral inhalation are active against influenza A and B viruses and are most effective in reducing severity of influenza illness when administered within 48 hours after illness onset. A 6-week oseltamivir regimen has a 92% efficacy against influenza illness among nursing home residents, and a 4-week zanamivir regimen is 83% effective among high-risk groups in the community. Zanamivir must be avoided in patients with underlying respiratory disease (e.g., asthma, chronic obstructive pulmonary disease). Amantadine and rimantadine are not recommended for treatment or prophylaxis of currently circulating viruses because of drug resistance. Inactivated influenza vaccine (not live vaccine) can be administered to patients who receive influenza antiviral drugs for treatment or chemoprophylaxis. Antiviral chemoprophylaxis does not impair the immunologic response to trivalent inactivated influenza vaccine. Treatment of influenza is further discussed in Chapter 17.

**Pneumococcal Disease**

Invasive pneumococcal disease (pneumonia, bacteremia, meningitis, endocarditis) is caused by Gram-positive, facultative, anaerobic *Streptococcus pneumoniae*. The organism accounts for up to 36% of community-acquired pneumonia cases and 50% of hospital-acquired pneumonia cases in the United States. The incidence of invasive disease ranges from 3.8 per 100,000 among persons aged 18–34 years to 36.4 per 100,000 among those aged ≥65 years. Vaccination is the most effective strategy for preventing invasive disease caused by the most common serotypes of *Streptococcus pneumoniae*. The Healthy People 2020 initiative aims to reduce the incidence of invasive pneumococcal infection to 31 per 100,000 persons in the elderly.

The ACIP recommends one-time pneumococcal vaccination to all persons who are 65 years or older, immunocompromised persons, and residents of nursing homes or other long-term care facilities. One-time revaccination is indicated for certain groups, including an elderly person who was vaccinated at least 5 years previously and was aged <65 years at the time of primary vaccination. All persons who have unknown vaccination status should receive one dose.
In addition, the ACIP recommends routine use of 13-valent pneumococcal conjugate vaccine (PCV13) for adults aged ≥19 years with immunocompromising conditions, functional or anatomic asplenia, cerebrospinal fluid leaks, or cochlear implants. Eligible adults who have not previously received PCV13 or the 23-valent pneumococcal polysaccharide vaccine (PPSV23) should receive a dose of PCV13 first, followed by a dose of PPSV23 at least 8 weeks later. A second PPSV23 dose is recommended 5 years after the first PPSV23 dose for persons aged 19–64 years with functional or anatomic asplenia and for persons with immunocompromising conditions. The pneumococcal vaccine is 50% to 80% effective for prevention of invasive pneumococcal disease among immunocompetent older adults and adults with various underlying illnesses. The 0.5-mL dose of PCV13 should be administered intramuscularly. PPSV23 should be administered intramuscularly or subcutaneously (also 0.5-mL dose) and may be administered at the same time with influenza or tetanus vaccine, provided that they are injected at opposite sites. The most common adverse effects are local site reaction, including pain, swelling, and erythema (15% to 60%). Asthenia, fatigue, and myalgia (12% to 13%) may occur. Persons with a severe allergic reaction to a vaccine component or following a prior dose should avoid further doses. Persons with moderate or severe acute illness should defer receiving the vaccine until the symptoms subside. Minor illness, such as upper respiratory infection, is not a contraindication to receiving the vaccine. The treatment of pneumonia is further discussed in Chapter 17.

Tetanus, Diphtheria, Pertussis

Tetanus is caused by Clostridium tetani spores, which are ubiquitous in the environment and enter the body after blunt trauma or deep puncture wounds. Its typical symptoms are trismus (lockjaw), generalized rigidity, and painful muscular and impaired respiratory function. Glottic spasm, respiratory failure, and autonomic instability can result in death. It has a reported case-fatality of 18% in the United States. Although tetanus is uncommon, older adults have a disproportionate burden of illness from tetanus. During 1999 and 2001, approximately 38% of 534 reported cases occurred in persons with age ≥65 years in the United States. From 1947 to 2008, the number of tetanus cases reported each year continued to decline. This decline was in part because of continued use of tetanus antitoxin for wound management and introduction of universal childhood immunization and tetanus boosters for adults. Sporadic cases of tetanus continue to occur in adults, especially in people who were not vaccinated in childhood or did not stay up to date on their 10-year booster shots. A dose of tetanus toxoid, reduced diphtheria toxoid, and acellular pertussis (Tdap) for older adults resulted in a moderate decrease in the number of cases and outcomes (e.g., outpatient visits, hospitalizations, and deaths). A one-time dose of Tdap to adolescents and adults also boosts immunity to pertussis and helps to prevent the transmission of pertussis to young children. This recommendation is particularly important to follow since the pertussis outbreaks in 2009 (more than 21,000 cases) and 2012 (more than 48,000 cases), which occurred mainly in infants younger than 1 year old. The ACIP recommends that all adults aged 19 years and older who have not yet received a dose of Tdap should receive a single dose. Tdap should be administered regardless of interval since last tetanus or diphtheria toxoid-containing vaccine. After receipt of Tdap, persons should continue to receive one tetanus booster dose every 10 years for adults who have completed a primary series. Adults with uncertain histories of a complete primary series of vaccines containing tetanus and diphtheria toxoids should begin or complete a primary three-dose series. Tetanus vaccine can be used after an exposure to tetanus, such as an injury. The tetanus booster has an efficacy of about 65%. The vaccine should be considered for those who are at risk for wounds or injuries and for institutionalized elderly who are at significant risk for cutaneous ulcers. It can be administered with other indicated vaccines, provided that each vaccine is administered using a separate
syringe at a different anatomic site. Contraindications in the elderly include serious allergic reactions or adverse effects with any tetanus-containing vaccines (Td, Tdap, DTP, DTap, or DT) or moderate or severe illness. The most common adverse effects are pain at the injection site (60% to 65%), followed by erythema, headache, tiredness, swelling, and generalized body ache.107

Herpes Zoster

Herpes zoster infection (shingles) is a localized, painful cutaneous eruption due to the reactivation of latent varicella zoster virus (chickenpox). The risk of zoster infection increases with advancing age. The annual incidence among adults age 50 is 2.5–5.1 cases per 1,000 persons and increases to 11–14 cases per 1,000 persons among those at 75 years.110,111 Zoster infection affects nearly half of persons age ≥85 at least once in a lifetime.112 Older adults are also more likely to experience postherpetic neuralgia, and with increased severity and duration.113 About 80% of postherpetic neuralgia occurs in zoster patients aged ≥50 years, who also report more persistent pain.114 In addition, persons aged 70–74 years and ≥85 years are 9 times and 23 times, respectively, more likely to require hospitalization due to zoster than younger persons.115

The ACIP recommends routine zoster vaccination of all persons aged ≥60 years for prevention of zoster infection, although the vaccine product is approved for persons aged 50 or older with certain risk factors (pre-existing chronic pain, severe depression, other comorbidities, intolerance to treatment medications).116,117 The vaccine is not indicated to treat acute zoster, to prevent persons with acute zoster from developing postherpetic neuralgia, or to treat ongoing postherpetic neuralgia. Persons with previous episodes of zoster and those with chronic medical conditions can be vaccinated unless those conditions are contraindications or precautions (Table 16-2). The vaccine is 51% effective for preventing zoster, although efficacy declines with increasing age, especially after 70 years. Use of this vaccine has also been linked with a reduction in the complications associated with herpes zoster, particularly postherpetic neuralgia.118

Zoster vaccine is a live attenuated vaccine and should be administered as a single 0.65-mL dose subcutaneously in the deltoid region of the arm.117,118 It may be given at the time of an inactivated vaccine provided that a different anatomic site is used. It should be given at least 4 weeks before or after another live attenuated vaccine. It is contraindicated for persons with a history of anaphylactic reaction to any component of the vaccine, including gelatin and neomycin. A history of contact dermatitis to neomycin is not a contraindication. The vaccine should be stored in a freezer with a separate sealing door at −15°C (+5°F) or colder. It should be reconstituted immediately on removal from storage and administered or discarded within 30 minutes. The common side effects with the vaccine are injection site reactions (17%), which include erythema, pain, swelling, warmth, and pruritus. Headache occurred in 9.4% of vaccine recipients.117,118

KEY POINT: Zoster vaccine should be offered to older adults (age ≥60) even if they had a previous episode of zoster, as long as they do not have contraindications to the vaccine. The vaccine recipients should be educated that the zoster vaccine prevents but does not treat zoster or postherpetic neuralgia.

Cancer Screening

Etiology and Epidemiology Specific to the Elderly Population

Despite much advancement we have achieved in technology and medicine, cancer remains one of the worst fears of humans and an important cause for morbidity and mortality in the world. The American Cancer Society (ACS) estimated
Cancer is associated with both external factors and internal factors. External factors include tobacco, chemicals, radiation, and infectious organisms (such as hepatitis B virus, human papillomavirus [HPV], HIV, Helicobacter pylori, and others). Internal factors consist of inherited mutations, hormones, immune conditions, and mutations that occur from metabolism. With age, a greater number of exposures to these factors may occur, thus increasing the risk of cancer development. In fact, most new cancers and cancer deaths occur in men and women older than 65 years of age. According to data derived from the National Cancer Institute Surveillance, Epidemiology, and End Results Program from 1998 to 2002, 56% of all newly diagnosed cancer patients and 71% of cancer deaths occur in this age group. Specifically, the median ages of cancer patients at death for major malignancies such as lung, colorectal, lymphoma, leukemia, pancreas, stomach, and urinary bladder range from 71 to 77 years. Thus, cancer affects older people to a much greater extent compared to younger adults, and it is important to educate the older as well as the general adult population regarding cancer prevention and screening.

**Table 16-2. Contraindications for Zoster Vaccine**

<table>
<thead>
<tr>
<th>Contraindications</th>
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<tbody>
<tr>
<td>• History of anaphylactic reaction to any component of the vaccine, including gelatin and neomycin.</td>
</tr>
<tr>
<td>• Leukemia, lymphomas, or other malignant neoplasms affecting the bone marrow or lymphatic system.</td>
</tr>
<tr>
<td>• AIDS or other clinical manifestations of HIV (persons with CD4+ T-lymphocyte values ( \leq 200 ) per mm(^3) or ( \leq 15% ) of total lymphocytes).</td>
</tr>
<tr>
<td>• Therapy with high-dose corticosteroids (( \geq 20 ) mg/day of prednisone or equivalent) for ( \geq 2 ) weeks.</td>
</tr>
<tr>
<td>• Clinical or laboratory evidence of other unspecified cellular immunodeficiency. However, persons with impaired humoral immunity (e.g., hypogammaglobulinemia or dysgammaglobulinemia) can receive zoster vaccine.</td>
</tr>
<tr>
<td>• Hematopoietic stem cell transplantation.</td>
</tr>
<tr>
<td>• Therapy with recombinant human immune mediators and immune modulators (adalimumab, infliximab, or etanercept).</td>
</tr>
<tr>
<td>• Pregnancy.</td>
</tr>
<tr>
<td>• Severe acute illness.</td>
</tr>
<tr>
<td>• Initiation of immunosuppressive therapy within 14–30 days.</td>
</tr>
<tr>
<td>• Therapy with antiviral in the past 24 hr.</td>
</tr>
</tbody>
</table>

a total of 1,665,540 new cases of cancer and 585,720 deaths from cancer in the United States in 2014. This translates to one in four deaths in the United States due to cancer. Among men, the three most common types of cancers that account for about 50% of all newly diagnosed cases are cancers of the prostate, lung and bronchus, and colorectum. In women, cancers of the breast, lung and bronchus, and colorectum are the three most commonly diagnosed types of cancers that account for about 50% of cases.

Fortunately, the combined death rate (deaths per 100,000 population) from cancer has been continuously declining for two decades. Mortality rates from cancer have decreased from a peak of 215.1 in 1991 to 171.8 in 2010. Of note, lung cancer death rate has declined 34% between 1991 and 2010 among men and 9% between 2002 and 2010 among women because of a reduction in tobacco use. In addition, a decrease in death rates for breast, prostate, and colorectal cancers (down from peak rates by 34%, 45%, and 46%, respectively) was credited to improvements in cancer screening and treatment.
Cancer Prevention and Screening Tests Applicable in the Geriatric Population

Cancer Prevention

Cancers caused by cigarette smoking, heavy use of alcohol, obesity, and excessive sun exposure are preventable. Based on evidence from the ACS, approximately one-third of the more than 500,000 cancer deaths that occur in the United States each year can be attributed to poor dietary and physical habits and could be prevented. In addition, another one-third of these 500,000 cancer deaths is caused by exposure to tobacco products and could also be avoided. Cancer prevention measures used in younger adults are also important to apply in geriatric populations. They include tobacco avoidance; diet, nutrition and physical activity; sun safety; and decreased exposure to radon.

Regular cancer screening can prevent cancers of the cervix, colon, and rectum by allowing removal of precancerous tissue before it becomes malignant. Regular screening can also lead to detection of cancers at early stages that increases their chance of being treatable. Malignancies that can be detected in their early stages include cancers of the breast, colon, rectum, cervix, prostate, oral cavity, and skin. For most of these cancers, early detection has been proven to reduce mortality. According to the ACS, cancers that can be prevented or detected earlier by screening account for at least half of all new cancer cases. Thus, there are ample opportunities as well as challenges for healthcare professionals to make positive impacts on their patients through proper cancer screening procedures. The following paragraphs describe cancer screening tests that are recommended by the ACS and the U.S. Preventive Services Task Force (USPSTF) for the detection of various cancers in the average-risk asymptomatic population. Patients with high risk for certain cancers (such as strong family history for colon or breast cancer) may require screening at an earlier time, at more frequent intervals, or genetic counseling. Interested readers are referred to the ACS and USPSTF guidelines for these special circumstances.

Breast Cancer Screening

Breast cancer is the most common cancer diagnosed in women in the United States. It is also the second leading cause of cancer death in U.S. women. The ACS guidelines for the early detection of breast cancer in average-risk women consist of a clinical breast examination and counseling to raise awareness of symptoms beginning at age 20; an annual mammogram beginning at age 40 is also recommended. Because false-positive results have been associated with breast self-examination (BSE), the ACS no longer recommends this monthly procedure. Instead, women may choose to perform BSE regularly, occasionally, or not at all based on information regarding the potential benefits, limitations, and harms (possibility of a false-positive result).

Women should be informed about the potential benefits as well as the potential harms associated with mammographic screening. Regular mammography may help to detect breast cancer in its early stage, thus allowing less aggressive therapy, a greater range of treatment options, and a greater chance for survival. On the contrary, limitations to mammography include false-positive result (which may lead to unnecessary biopsies, exposures to futile treatment, and emotional distress) and false-negative results (the inability to detect about 5% of breast cancer). Furthermore, some breast cancer detected with mammography may still have poor prognoses.

Because breast cancer grows faster in younger women compared to older women, the ACS recommends annual screening to women
in their forties. However, some data suggest that women 50 and older may be able to wait as long as 2 years between mammograms.\textsuperscript{141} There is no specific upper age at which mammography screening should be discontinued, according to the ACS.\textsuperscript{135} The decision to stop regular mammography screening should be individualized based on the potential benefits and risks of screening along with considerations of overall health and estimated longevity of the patient.\textsuperscript{135} Therefore, a woman should continue to receive regular mammography screening as long as she is in good health and would be a candidate for breast cancer treatment.\textsuperscript{135} In contrast to the ACS recommendations, the USPSTF recommends against routine screening mammography in women aged 40–49 years. In addition, the USPSTF recommends biennial (every 2 years) screening mammography for women 50–74 years of age and has no recommendation for women 75 years of age or older.\textsuperscript{136}

\textbf{Colorectal Cancer Screening}

Colorectal cancer (CRC) is the third leading cause of cancer death in the general U.S. population.\textsuperscript{119} Fortunately, it is also one of the most preventable cancers. Screening can lead to the detection and removal of adenomatous polyps before they transform into cancers. CRC screening can also detect cancers at earlier stages, increase survival, and reduce mortality rate.\textsuperscript{142} Given that 90\% of all cases of colon cancer occur after age 50, the ACS recommends that clinicians screen men and women 50 years of age or older for CRC.\textsuperscript{135}

The CRC screening tests are classified into two types: those that primarily detect cancer, such as the guaiac-based fecal occult blood test (gFOBT), fecal immunochemical test (FIT), and the stool DNA test; and those that detect cancer and advanced lesions (such as endoscopic and radiographic exams). The ACS has suggested several methods for colorectal screening\textsuperscript{135}:

- Annual gFOBT and FIT, following manufacturer's recommendations for specimen collection
- Flexible sigmoidoscopy every 5 years
- Colonoscopy every 10 years
- Double contrast barium enema every 5 years
- Computed tomographic colonography every 5 years

Although definitive evidence is lacking, colonoscopy may be superior to other screening methods because it gives a view of the entire colon and allows biopsy specimens to be taken immediately.\textsuperscript{143} Similar to breast cancer screening, there is no specific upper age limit in screening for CRC according to the ACS.\textsuperscript{135} Clinicians should educate patients on the risks, benefits, and proper usage of take-home screening tests. For example, in order to maximize the accuracy of the gFOBT or FIT, patients should be advised regarding the importance of commitment to annual at-home testing and adherence to the manufacturer's instructions. Patients should also be informed about the potential risks and adverse effects of certain procedures. Although the risk of colon perforation with colonoscopy was less than 0.5\% in patients 75 years and older according to a study that examined 39,286 colonoscopies, it was still four times the risk compared to patients in the 65 to 69 age range.\textsuperscript{143,144} Older patients may also have more difficulties tolerating adverse effects such as vomiting, abdominal cramps, and diarrhea from bowel preparations. Newer bowel preparations that require less fluid volume intake (i.e., approximately 2.2 L for Prepopik versus 4.0 L for Golytely) may increase patient adherence to complete the full preparation. However, it is unclear if these new bowel preparations are more tolerable in the geriatric population. CRC screening in older patients may be individualized by balancing the likelihood of finding polyps and the time for neoplastic transformation of a polyp against the patient's estimated life expectancy.\textsuperscript{143} Because few polyps transform into cancer in less than 10 years, patients with a life expectancy less than 7–10 years may not benefit from detection and removal of precancerous polyps.\textsuperscript{143} In contrast to the ACS recommendations, which do
not state an upper age limit for CRC screening, the USPSTF does not recommend routine CRC screening for adults 76–85 and recommends against screening for adults older than 85.\textsuperscript{135,137}

Cervical Cancer Screening

Over 12,000 women are diagnosed with invasive cervical cancer with over 4,000 deaths from this disease annually.\textsuperscript{135} Because screening can prevent cancers of the cervix by allowing removal of precancerous tissue before it becomes malignant, the ACS and the USPSTF recommend screening for cervical cancer in women age 21 to 65 years of age. Infection with high-risk oncogenic types of HPV has been implicated as the cause of 100% of cervical cancer.\textsuperscript{145} Due to the long latency between infection and development of cervical cancer, older women with at least two negative Pap smear results and no evidence of HPV infection may be at extremely low risk for cervical cancer.\textsuperscript{121} For this reason, the ACS and the USPSTF recommend discontinuation of screening in older women at average risk when Pap test results have been normal. At this time, the USPSTF recommends against routine screening of women older than age 65 for cervical cancer if they have had adequate recent screening with normal Pap smears and are not otherwise at high risk for cervical cancer.\textsuperscript{138} The ACS recommends discontinuation of cervical cancer screening after age 65 years if three consecutive negative cytology tests or two consecutive negative co-tests (HPV testing and cytology) results were obtained within the 10-year period prior to stopping screening, with the most recent test performed within the last 5 years.\textsuperscript{135}

Prostate Cancer Screening

Prostate cancer is the most common non-skin cancer and the second leading cause of cancer-related death in U.S. men.\textsuperscript{119,139} Approximately 233,000 men receive a new diagnosis of this disease annually, and it is estimated that one in six men will be diagnosed with prostate cancer in his lifetime.\textsuperscript{135,139} Two screening tests, the prostate-specific antigen (PSA) test and the digital rectal examination (DRE), have been used to detect prostate cancer. Although the PSA test is more sensitive than the DRE and has been used frequently for the screening of prostate cancer, it is not specific to prostate cancer. Besides prostate cancers, common conditions such as benign prostatic hyperplasia and prostatitis can increase PSA levels.\textsuperscript{146} Thus, false-positive results can occur from PSA screening tests that may lead to painful experiences through unnecessary prostate biopsy as well as emotional distress.

In men who are diagnosed with prostate cancer, treatment can cause harms such as sexual dysfunction, bowel and bladder incontinence, and death.\textsuperscript{147} Furthermore, a proportion of those treated, and possibly harmed, would never have developed cancer symptoms during their lifetime, thus leading to unnecessary treatment and associated adverse effects.\textsuperscript{146,147} Based on these findings, the USPSTF recommends against PSA-based screening for prostate cancer in the general U.S. male population, regardless of age.\textsuperscript{139} In contrast, the ACS states that men at average risk beginning at age 50 years who have a life expectancy of at least 10 years should have an opportunity to make an informed decision with their healthcare provider about prostate cancer screening.\textsuperscript{135} More importantly, clinicians should discuss the potential benefits, limitations, and known harms of PSA screening with their patients.\textsuperscript{135,147} Individualized screening decisions should be made based on shared decision (between clinicians and patients) or patients’ preferences.\textsuperscript{135,147}

Lung Cancer Screening

Lung cancer is the second most common newly diagnosed cancer and the leading cause of cancer-related deaths in America.\textsuperscript{119,140} It is estimated that 224,210 new cases of lung cancer and 159,260 deaths related to lung cancer occur in the United States annually.\textsuperscript{119} In an effort to find an effective approach to detect lung cancer in its early stage, the National Lung Screening Trial (NLST) compared the effectiveness of annual low-dose helical computed tomography (LDCT) to annual chest x-ray (CXR) in 53,454
Due to observations from the NLST, the USPSTF and ACS now recommend lung cancer screening in older adults at high risk of lung cancer because of smoking or a history of smoking. Specifically, the USPSTF recommends annual screening for lung cancer with LDCT in adults aged 55–80 years who have a 30 pack-year smoking history and currently smoke or have quit within the past 15 years. The USPSTF further stated that screening should be stopped once a person has not smoked for 15 years or develops a health condition that substantially limits life expectancy or the ability or willingness to have curative lung surgery. In comparison, the ACS urges clinicians with access to high-volume, high-quality lung cancer screening and treatment centers to initiate a discussion regarding lung cancer screening with patients aged 55–74 years who are in relatively good health and have at least a 30 pack-year smoking history, currently smoke, or have quit within the past 15 years. Importantly, the benefits, uncertainties, and harms associated with screening for lung cancer with LDCT should be included in the discussion.

Cancer-Related Checkup

At this time, the ACS and the USPSTF endorse population screening for cancers of the cervix, breast, and colon and rectum. For the average-risk elderly population, the best approach to cancer prevention may be through periodic health evaluations. The accessibility of healthcare through primary care physicians has been associated with a higher rate of early breast, cervical, and colon cancer detection. Regular preventive health examinations provide opportunities for health counseling, cancer screening, and case-finding examinations of the thyroid, testicles, ovaries, lymph nodes, oral cavity, and skin. In addition, shared decision making about cancer screening for early cancer for sites where population-based screening is not yet recommended can be explored.

**KEY POINT:** Periodic health examination provides a good opportunity for health counseling and cancer screening that could lead to prevention and early detection of cancer.

**Common Concerns with Cancer Screening in Elderly Patients**

Although the incidence of cancer development is greater in older adults, cancer screening may not always be beneficial because of a number of concerns faced by this population. These concerns include complications from additional diagnostic procedures due to inaccurate test results, identification and treatment of clinically unimportant cancers, and psychological as well as physical distress from screening. A false-positive diagnosis can lead to pain and emotional stress from additional biopsies and procedures. In the case of prostate cancer screening, men with false-positive PSA test results were more likely to worry specifically about prostate cancer, have a higher perceived risk of prostate cancer, and report problems with sexual function compared with control participants for up to 1 year after the test. As life expectancy decreases in the elderly, the probability of finding inconsequential cancer increases. Thus, the identification of cancer that would never have caused symptoms in the patient's lifetime could lead to unnecessary treatment and associated adverse effects. Finally, elderly patients may have cognitive, physical, or sensory dysfunctions that make screening tests and further workup particularly difficult, painful, or frightening. Concerns for cancer screening have also been addressed by the American Geriatrics Society and the American Board of Internal Medicine Foundation through the Choosing Wisely campaign.
Fundamentals of Geriatric Pharmacotherapy

Recommendations from this campaign do not encourage screening for breast, colorectal, or prostate cancer without considering life expectancy and the risks of testing, overdiagnosis, and overtreatment.\textsuperscript{153} Specifically, the recommendations state that screening for these three cancers exposes patients to immediate harms with little chance of benefit in those with a life expectancy of less than 10 years.\textsuperscript{153}

In contrast to the above scenarios, the decision not to screen a particular individual based on health status or life expectancy may lead to a decrease in quality of life.\textsuperscript{121,154} The decision to screen elderly people for cancer can be complex and is based on many factors other than survival benefit alone.\textsuperscript{154} Clinicians should discuss the benefit, risk, and limitations of each screening test with the patient. Decisions on choosing cancer screening should be individualized based on the life expectancy of the patient, the risk versus benefit associated with screening, and the preferences of the patient or his or her caregiver.\textsuperscript{121,154}

**KEY POINT:** Some older patients may not benefit from cancer screening tests due to factors such as decreased life expectancy, decreased physical functions, and/or comorbid conditions.

Evidence Supporting Cancer Prevention Medications and Supplements

Cancer chemoprevention is defined as the use of natural, synthetic, or biologic chemical agents to reverse, suppress, or prevent carcinogenic progression to invasive cancer.\textsuperscript{155} In an attempt to prevent the development or progression of cancer, substances such as vitamins, pharmaceutical products, and herbal remedies have been examined. The following paragraphs briefly describe some of the vitamins and medications that have been tested for the prevention of various cancers. Interested readers are referred to more comprehensive review literature on cancer chemoprevention.\textsuperscript{155-157}

**Breast Cancer Chemoprevention**

Chemoprevention trials in breast cancer have set the standard for other disease types to follow.\textsuperscript{155} Tamoxifen is an oral selective antiestrogen agent or selective estrogen receptor modulator (SERM). This medication is most commonly used as a treatment for women with estrogen receptor positive (ER+) breast cancer. In addition, tamoxifen is indicated for risk reduction in women at high risk for breast cancer. Meta-analyses from various trials showed that tamoxifen reduced the rate of contralateral breast cancers by 40% to 50% in women with ER+ tumors.\textsuperscript{155} This beneficial effect was confirmed in a placebo-controlled trial, the Breast Cancer Prevention Trial, which studied 13,388 women. It was stopped early after an interim analysis showed a significant 49% reduction in incidence of invasive breast cancer in the tamoxifen arm.\textsuperscript{155} Similar to findings from earlier meta-analyses, only ER+ tumors were affected (69% decrease) by tamoxifen. With regard to adverse effects, an increased risk of invasive endometrial cancer and thrombotic events (especially in women age 50 and older) were observed. Thus, the use of tamoxifen as chemoprevention for breast cancer should be highly individualized based on the potential risk and benefit to the patient.\textsuperscript{155}

Raloxifene is a SERM indicated for the treatment and prevention of osteoporosis in postmenopausal women. It also has an FDA-approved indication for the risk reduction of invasive breast cancer in postmenopausal women with osteoporosis or in women at high risk for invasive breast cancer. In their reports of results from the study of tamoxifen and raloxifene, researchers stated that tamoxifen and raloxifene lowered the risk of invasive breast cancer to a similar extent in 19,747 postmenopausal women who took raloxifene 60 mg or tamoxifen 20 mg daily for 5 years.\textsuperscript{158,159} The observed incidence rates of invasive breast cancer were raloxifene 4.4 and tamoxifen 4.3 per 1,000 women per year.\textsuperscript{159} Women on both drugs had similar risks
for strokes and heart attacks. Raloxifene did not protect women from lobular carcinoma in situ and ductal carcinoma in situ as well as did tamoxifen. However, women on raloxifene had fewer uterine cancers and blood clots than women on tamoxifen. Based on available information, chemoprevention with either tamoxifen or raloxifene may best be used in a woman who has a higher than average risk of breast cancer and who is willing to accept the risk of harm from long-term use (up to 5 years) of these medications. Both potential benefits and potential harm must be considered in the decision-making process.

Exemestane, an aromatase inhibitor, has also shown benefits in breast cancer prevention in postmenopausal women. The effectiveness of exemestane was compared to that of placebo in a trial that involved 4,560 postmenopausal women with a median Gail risk score of 2.3%. At a median follow-up of 35 months, 11 and 32 invasive breast cancers were detected in the exemestane group and in the placebo group, respectively. This represents a 65% relative reduction in the annual incidence of invasive breast cancer in the exemestane group compared to the placebo group (0.19% versus 0.55%; \( P = 0.002 \)). The annual incidence of invasive plus noninvasive breast cancers was also observed to be lower in the exemestane group compared to the placebo group (0.35% versus 0.77%; \( P = 0.004 \)). Adverse events were more common in the exemestane group compared to the placebo group (88% versus 85%; \( P = 0.003 \)) with menopausal symptoms such as hot flashes, fatigue, sweating, insomnia, and arthralgia being the most common adverse effects experienced by women in this trial. Additional placebo-controlled trials in healthy women and patients with early breast cancer to evaluate prolonged aromatase-inhibitor therapy in postmenopausal women are currently ongoing.

Phytoestrogens are a group of plant-derived substances that are structurally or functionally similar to estradiol. These substances are thought to have protective effects against breast cancer because a decreased risk of breast cancer was observed in women from countries with high phytoestrogen consumption. Studies show that soy exposure during a woman’s adolescent years appears to be protective. However, results of studies that examine effects of adult exposure to phytoestrogens are conflicting and inconclusive. Furthermore, data on the role of phytoestrogens in the prevention of breast cancer recurrence are scarce, and the few studies conducted do not support a protective role. For these reasons, supplemental intake or augmentation of dietary phytoestrogen sources is not recommended. Consumption of naturally occurring soy products such as tofu or soy flour as part of a balanced diet low in saturated fats and high in fruits and vegetables is likely safe and may be beneficial.

Colon Cancer Chemoprevention

Aspirin is a promising medication for colon cancer chemoprevention and has been studied in several large randomized trials for the prevention of colon adenomas and cancer. In a randomized double-blind trial conducted by Baron et al., daily aspirin (325 or 81 mg) or placebo was given to 1,121 patients with a recent history of colon adenomas. Results showed that low-dose aspirin prevented recurrence of colorectal adenomas to a greater degree compared to the other two regimens (incidence of one or more adenomas was 47% in placebo, 38% in the aspirin 81-mg group, and 45% in the aspirin 325-mg group). This translated into a relative-risk reduction of 19% in the aspirin 81-mg group and a nonsignificant reduction of 4% in the aspirin 325-mg group when compared with placebo. Furthermore, a relative risk reduction of 40% for advanced neoplasms was observed in the aspirin 81-mg group and a nonsignificant reduction of 4% in the aspirin 325-mg group when compared with placebo. Aspirin at a daily dose of 300 mg or higher has shown protective effects in the prevention of colorectal adenomas and CRC in other studies. In a recent pooled analysis of two large trials (The British Doctors Aspirin Trial and the United Kingdom Transient Ischaemic Attack Aspirin Trial) that involved more than 7,500 patients, use of 300 mg or more of aspirin daily for about 5 years was found to be effective in the primary prevention of CRC.
Contrary to the above findings, the U.S. Physician’s Health Study, which included 22,071 male physicians with a mean follow-up of 5 years, reported that regular use of low-dose aspirin had no effect on the incidence of polyps or colon cancer.\(^{167}\) Although aspirin has shown encouraging results in decreasing colorectal adenomas in some trials, this effect was not consistent, and the optimal dose for colon protective effect seemed unclear. This suggests that aspirin use cannot be a substitute for colon surveillance and that further studies are needed for effective colon cancer chemoprevention.\(^{155}\)

Calcium and vitamin D supplementation have been the focus of CRC prevention in a number of studies.\(^{168-171}\) Calcium is thought to prevent colorectal carcinoma by binding bile and fatty acids as well as inhibiting the proliferation of colonic epithelial cells.\(^{155,172}\) Calcium supplementation was shown to moderately reduce colorectal adenomas in some studies.\(^{168-170}\) However, at this time it is unclear whether calcium supplementation translates into prevention of invasive CRC and a survival benefit.\(^{155}\) In addition to maintaining bone health, evidence showed that vitamin D may have a role in CRC prevention.\(^{173}\) Low levels of vitamin D have been associated with increased risk of digestive-system cancers in men.\(^{171}\) In addition, vitamin D was shown to play an important role in promoting the effects of calcium in reducing the risk of colorectal adenoma recurrence.\(^{170}\) The new 2010 recommended daily allowance for vitamin D is 600 international units for individuals 1–70 years of age and 800 international units for adults 71 years of age and older. It is unclear whether these dosage recommendations are sufficient to provide the possible cancer protective effect of vitamin D. In fact, many experts have recommended doses of vitamin D as much as 1,000 international units daily for optimal health.\(^{173}\) Of note, the ACS does not have a recommendation regarding the role of vitamin D in cancer prevention or treatment.\(^{173}\)

A diet that is filled with fiber-rich foods may decrease the risk of CRC. Dietary fiber decreases transit time of food through the gastrointestinal tract.\(^{174}\) It also enhances bacterial fermentation that leads to increased production of short-chain fatty acids such as acetate, propionate, and butyrate.\(^{174}\) In rats, these substances have been found to induce apoptosis in CRC cells.\(^{174}\) The European Prospective Investigation into Cancer and Nutrition examined the association between dietary fiber intake and incidence of CRC in more than 500,000 participants.\(^{175}\) Results of this study showed that dietary fiber in foods was inversely related to the incidence of large bowel cancer (adjusted relative risk 0.75 [95% CI 0.59–0.95]), for the highest versus lowest quintile of intake.\(^{175}\) Furthermore, findings from this study suggested that doubling of total fiber intake in individuals with low average intake of dietary fiber could reduce the risk of CRC by 40% in this population.\(^{175}\) Based on the current data regarding the possible benefit of dietary fiber in reducing the risk of CRC, meals that are rich in fiber as well as protective phytochemicals (such as fruits and legumes, especially cruciferous and green leafy vegetables) have been recommended to impact the prevalence of this disease.\(^{174}\)

**Lung Cancer Chemoprevention**

Various agents, such as beta carotene, alpha-tocopherol, aspirin, isotretinoin, and N-acetylcysteine have been tested in lung cancer chemoprevention trials.\(^{155}\) Unfortunately, no chemoprevention agents have clearly demonstrated clinical benefit in lung cancer to date.\(^{155}\) Because fruit and vegetable consumption have been associated with a reduced risk of cancer, attempts have been made to isolate specific nutrients and administer them as supplements for cancer prevention. However, a higher rate of lung cancer was found in cigarette smokers who took high-dose beta carotene supplements in two clinical trials.\(^{176,177}\) This points to the perception that beta carotene may only be a proxy for other single nutrients or combinations of nutrients found in whole foods, and that taking a single nutrient in large amounts can be dangerous.\(^{123}\) Thus, consuming fruits and vegetables that contain beta carotene may be beneficial, but high-dose beta carotene supplements should be avoided.\(^{123}\)
Prostate Cancer Chemoprevention

Finasteride, a 5 alpha-reductase inhibitor (5ARI), has shown some promise in the prevention of prostate cancer. In the Prostate Cancer Prevention Trial (PCPT), 18,882 men age 55 or older with a normal DRE and a PSA level of 3.0 ng/mL or lower were randomized to finasteride 5 mg per day or placebo for 7 years.\(^{178}\) This trial reported 18.4% of prostate cancer incidence in the finasteride group compared to 24.4% in the placebo group, for a 24.8% reduction in prevalence over the 7-year period that was statistically significant.\(^{178}\) Patients who received finasteride also experienced fewer urinary symptoms compared to the placebo group. However, the prostate cancers that developed in the finasteride group were of higher Gleason grade (7, 8, 9, or 10), and patients who received finasteride also had more adverse sexual side effects.\(^{178}\)

Dutasteride, another 5ARI, was more recently evaluated as chemoprevention for prostate cancer in the Reduction by Dutasteride of Prostate Cancer Events trial.\(^{179}\) This trial randomized 8,231 men aged 50–75 years with a PSA concentration of 2.5–10 ng/mL and one negative prostate biopsy within 6 months before enrollment to either dutasteride 0.5 mg daily or placebo. Results showed a diagnosis of prostate cancer in 19.9% of men in the dutasteride group and 25.1% of men in the placebo group, representing a relative risk reduction with dutasteride of 22.8% over the 4-year study period.\(^{179}\) In contrast to observations from the PCPT, no overall significant increases in high-grade prostate cancers were found in the dutasteride group compared with the placebo group in years 1 through 4 of the study. Similar to finasteride, dutasteride therapy was associated with a reduced rate of urinary retention but an increased incidence of sexual side effects when compared with placebo.

At present, neither finasteride nor dutasteride has received an approved indication for use in risk reduction of prostate cancer. This decision by the FDA was due in part to concern about a possibly higher incidence of high-grade prostate cancer in patients receiving a 5ARI.\(^{180}\) Further studies are needed to clarify the role of finasteride and dutasteride in chemoprevention for prostate cancer.\(^{180}\)

**KEY POINT:** The decision to use certain medications for chemoprevention should be individualized based on the risk and benefit for each person.

Nutrition may play a role in reducing the risk of prostate cancer. Frequent intake of tomato products that contain lycopene has been associated with a lower risk of prostate cancer.\(^{181}\) Foods that contain specific antioxidant nutrients, such as vitamin E, selenium, and beta carotene may also have protective effects in prostate cancer.\(^{123}\) On the contrary, greater consumption of red meat or dairy products may be associated with an increased risk of prostate cancer.\(^{123,182}\) A high calcium intake, primarily through supplements, has also been associated with increased risk for more aggressive types of prostate cancer.\(^{183}\) Based on the data available at this time, the best way to reduce prostate cancer risk may be through consuming five or more servings of a wide variety of fruits and vegetables each day, limiting intake of red meats and dairy products, and maintaining an active lifestyle and healthy weight.\(^{123}\)

**KEY POINT:** Consumption of fruits and vegetables that contain certain vitamins such as beta carotene may be beneficial, but high-dose vitamin supplementation should be avoided.
CASE 1: ANEMIA

Setting:
Long-term care nursing facility.

Subjective:
RO is a 74-year-old woman who has been in a skilled nursing facility for about 18 months. She was originally admitted following an accident in which she slipped on a wet floor and broke her hip. She has been ambulating well with the use of a walker for about the last 6 months and is in good overall spirits with a good appetite. She recently has been complaining of fatigue and lethargy, so her physician ordered a complete blood count that showed anemia. Other laboratory work was ordered to evaluate the type of anemia. RO’s physician asks for you to proceed with treatment as appropriate under your collaborative practice agreement.

Past Medical History:
Type II diabetes, hypothyroidism, osteoarthritis, and chronic kidney disease.

Medications:
Glipizide 10 mg once daily, aspirin 81 mg once daily, simvastatin 10 mg once daily, pioglitazone 45 mg once daily, levothyroxine 75 mcg once daily, acetaminophen 500 mg four times daily, geriatric multivitamin with minerals.

Allergies:
NKDA.

Social History:
Negative for smoking, alcohol, or recreational drugs.

Family History:
Noncontributory.

Objective:
Ht 5’2˝, Wt 118 lb, BP 122/68 mmHg, P 72 BPM, T 98°F, RR 14/min, pain 4/10 at both knees.

Physical Examination:
Unremarkable other than decreased range of motion and crepitus in her knees. There is no evidence of bleeding.

Labs:
BUN 38; serum creatinine 1.6 mg/dL (BUN 30, Scr 1.4 3 months ago); potassium 4.1 mmol/L; hemoglobin 9.5 g/dL; hematocrit 28.5%; MCV 92 fl; hemoglobin A₁c 7.2%; TSH 1.3 milli-International Units/L; Fe 29 mcg/dL, TIBC 161%, ferritin 815 ng/mL, folate 5.11 ng/mL, vitamin B₁₂ 791 ng/mL.

Assessment:
RO is a 74-year-old female with diabetes, hypothyroidism, osteoarthritis, and chronic kidney disease who offers new complaints of fatigue and lethargy consistent with anemia. She has no signs of bleeding, and her hypothyroidism is well controlled. Her hemoglobin is low, with a normal MCV. Vitamin B₁₂ and folate are normal. Iron studies are consistent with anemia of chronic kidney disease.
Plan:
1. Initiate epoetin alpha 3,000 units subcutaneously three times a week. Adjust dose to achieve a hemoglobin target between 10 and 11.5 g/dL.
2. Initiate oral ferrous sulfate 325 mg daily. Consider parenteral iron therapy if response is inadequate based on hemoglobin and iron studies.
3. Repeat hemoglobin twice weekly for dosage adjustments. Measure ferritin in 1 month.

Rationale:
1. ESA is the treatment of choice for anemia of chronic kidney disease, generally initiated at 50–100 units/kg three times weekly. Dosage requires adjustment to maintain the hemoglobin at or below 11.5 g/dL.
2. Geriatric multivitamins do not contain iron, and RO’s iron and ferritin levels will drop with initiation of ESA. Iron therapy should be initiated in conjunction with ESA to allow for maximal effect. Oral ferrous sulfate is frequently chosen, but doses over 325 mg daily are not recommended due to a significant risk for constipation with higher doses without much more absorption. Parenteral iron therapy is more effective than oral iron therapy for anemia of chronic kidney disease and improves the response to ESAs, so it should be considered if RO does not respond as expected to ESAs.
3. In all forms of anemia, monitoring for therapeutic response requires a complete blood count for hemoglobin and hematocrit. Frequent testing is required with use of ESAs to adjust to the proper dose that will minimize risk for thrombosis and maximize cost effectiveness.

Case Summary:
As in this case, anemia can present very subtly in the elderly patient, with symptoms that many attribute simply to old age. Clinicians must remain vigilant to identify the causes of anemia, as it is not a normal consequence of aging. Anemia of chronic kidney disease is common in older patients as renal function declines but may occur in combination with nutritional anemias or other anemias of chronic disease. Appropriate therapy addressing the cause(s) of anemia require monitoring, particularly when ESAs are initiated, to avoid the risks of thrombosis and stroke associated with higher hemoglobin levels.
Case 2: Immunization and Cancer Prevention

Setting:
Geriatric outpatient clinic.

Subjective:
MJ is a 70-year-old man who comes to the clinic in March to establish primary care and get a flu shot. He has moved from out of state to be closer to his daughter (age 35) and grandchildren (ages 4 and 10) 2 months ago. MJ asks if “it is too late to get a flu shot now.” He expresses concern about his family history of prostate cancer. He heard about “a prescription drug to stop it from happening to him.”

Past Medical History:
Hypertension, dyslipidemia, osteoarthritis, chronic obstructive pulmonary disease.

Immunizations:
10/1/2011: Pneumococcal vaccine (PPV23)
10/1/2011: Trivalent influenza vaccine (standard dose)
3/1/2003: Tetanus (Td) booster. He has completed the primary series of tetanus, diphtheria, and pertussis. Never received Tdap.

Medications:
Hydrochlorothiazide 12.5 mg daily, aspirin 81 mg daily, atorvastatin 10 mg at bedtime, albuterol/ipratropium 2 puffs every 4 hours, acetaminophen 650 mg every 6 hours as needed for knee pain.

Allergies:
NKDA.

Social History:
Married to wife ×45 years. Social alcohol consumption (2 drinks per week). Reports smoking 2 packs per day for 20 years and quit 11 years ago.

Family History:
Father died from prostate cancer at age 60. Mother died from car accident at age 70. Brother recently diagnosed with prostate cancer at age 65.

Objective:
Wt 160 lb, Ht 5’9”, BP 140/80 mmHg, labs all within normal limits.

Assessment:
MJ is a 70-year-old man who is past due for his annual influenza vaccine, usually given early in October or November. He is indicated to receive one dose of Tdap to replace tetanus booster dose and to prevent the transmission of pertussis to young family members who are at risk. He has a strong family history for prostate cancer.

Plan:
1. Give intramuscular influenza vaccine.
2. Offer Tdap and Zoster vaccine.
3. Advise patient that there is no approved prescription drug for the prevention of prostate cancer. Suggest he discuss the literature with his physician because new trials have shown possible benefit in specific types of patients. Offer education on lifestyle interventions, such as consuming five or more servings of a wide variety of fruits and
vegetables daily, limiting intake of red meats and dairy products, maintaining an active lifestyle and healthy weight, and avoiding high-dose vitamin supplements such as beta carotene.

Rationale:
1. MJ should receive a dose of influenza vaccine because of his age (>50), presence of chronic pulmonary disease, and household contact of children aged <5 years. He may receive any one of the intramuscular influenza vaccine products that are still available at the clinic (standard-dose trivalent, high-dose trivalent, or quadrivalent). Neither intradermal inactivated trivalent nor intranasal live attenuated quadrivalent vaccines are indicated for him.

2. The ACIP recommends that all adults age 19 years and older who have not yet received a dose of Tdap to receive a single dose. It should be administered regardless of interval since last tetanus or diphtheria toxoid-containing vaccine. This dose can also boost immunity against pertussis and prevent the transmission of pertussis to his grandchildren. After this dose of Tdap, MJ should continue to receive one Td booster dose every 10 years. He does not have any contraindications to zoster vaccine, and it is recommended to receive a lifetime single dose due to his age. MJ is up to date with pneumococcal vaccine (one dose of PCV23 after the age of 65). PCV13 is not indicated because he does not have any immunocompromised conditions, functional or anatomic asplenia, cerebrospinal fluid leaks, or cochlear implants. Note: The 2014 ACIP guideline recommends PCV13 in addition to PCV23 for all adults age 65 or older.

3. Although finasteride and dutasteride have been shown to reduce the incidence of prostate cancer in clinical trials, they are not approved for use in risk reduction of prostate cancer because of concerns of a possible higher incidence of high-grade prostate cancer. MJ should be informed of the risks and benefits of these drugs, and the decision to start chemoprevention should be individualized. In general, maintaining an active and healthy lifestyle should be emphasized.

Case Summary:
Immunization is an essential part of preventive medicine in geriatric care, especially older adults who may become caregivers of young children in the family. Annual influenza vaccine should be given until the supply is exhausted because influenza outbreaks may occur beyond the typical influenza season. Older adults should be screened for one-dose Tdap administration, especially when they have close household contacts with young children. Although chemoprophylaxis could be offered based on individual patient factors, maintaining an active and healthy lifestyle is often a good start for cancer prevention and health maintenance.
Clinical Pearls

- Injectable vitamin B12 is often supplemented in patients for a placebo effect such as a boost in vitality. In a community setting, use of this product is often a matter of patient choice. In the long-term care setting, if the clinical record does not contain a clearly documented indication for vitamin B12, such as pernicious anemia, regulations may dictate that its use in an injectable form be cited as an unnecessary medication without supporting indication. Therefore, the care plan should clearly provide documentation if the use of this supplement is the patient’s request.

- Patients with diabetes age 60 years and older may be vaccinated with hepatitis B vaccine based on the increased need for assisted blood glucose monitoring in long-term care facilities, likelihood of acquiring hepatitis B infection, need to manage its complications or chronic sequelae, and likelihood of immune response to vaccination. Clinicians should be proactive in offering hepatitis B vaccination to older adults with diabetes.

- Almost all reported cases of tetanus are in people who either have never been vaccinated or those who completed a primary series but have not had a booster in the previous 10 years. It is essential for clinicians to obtain records of immunization history. Unvaccinated patients should be given the opportunity to catch up with primary series or boosters.

Chapter Summary

The common types of anemia seen in the elderly are nutritional, chronic disease, and unexplained anemia, with these three types seen with almost equal prevalence. Complications due to anemia in older adults are high and can be rather severe even at what many would consider to be very mild reductions in hemoglobin. More research is sorely needed in the elderly anemic population to define an optimal hematologic treatment goal and help identify optimal treatment regimens that are specific for this population.

Elderly persons are at risk for influenza, pneumococcal disease, tetanus, and herpes zoster and should receive these vaccines unless contraindications exist. The ACIP recommends strategies to improve vaccination levels, including using reminder/recall systems and standing orders programs, administering vaccines during hospitalization or routine healthcare visits, providing vaccines in alternative settings, including pharmacies, and to provide publicity and education to reach potential vaccine recipients.

As our population of older men and women increases, more people will be confronted with cancer, as this disease mostly affects individuals over 65. Fortunately, a number of cancers can be prevented through proper dietary and physical habits. Furthermore, cancer screening can prevent or provide early diagnosis that leads to better prognosis for some cancers. At this time, most positive outcomes from screening are derived from detecting cancers of the cervix, breast, and colon and rectum. In spite of the many potential benefits from cancer screening, certain older individuals may not benefit from cancer screening because of decreased life expectancy, decreased physical functions, and comorbid diseases. Thus, a decision about cancer screening should be based on factors such as benefit, risk, and patient preferences rather than on survival benefit alone.
Self-Assessment Questions

1. What are the most common causes of anemia in the elderly?
2. What are the standard pharmacologic options (drugs and dosages) for treating nutritional anemia?
3. What is the rationale for the use of ESAs in the treatment of anemia and which anemia are they used to treat?
4. What are some complications that can occur in an elderly patient as a consequence of anemia?
5. What is the current ACIP recommendation on influenza, pneumococcal, tetanus, and zoster vaccines for a 65-year-old?
6. What are the efficacies and adverse effects of influenza, pneumococcal, tetanus, and zoster vaccines?
7. What are contraindications and precautions for live zoster vaccine?
8. What are the various cancer screening tests recommended by the ACS and the USPSTF for the general population?
9. What are cancer prevention measures that most people can adapt?
10. What are some medications that have shown promise in the prevention of cancer?

References


Infections and Antimicrobial Stewardship

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Learning Objectives

1. Describe age-related biomedical changes in the immune system that alter the risk for infection.
2. Recognize atypical presentation of infectious diseases and confounding factors of infection diagnosis among frail elderly.
3. Apply optimal geriatric assessment criteria to differentiate infection from other possible illnesses.
5. Design drug therapy regimens for common infectious diseases, including appropriate considerations for dose, duration, special administration, or monitoring needs based on age or frailty.

Key Terms and Definitions

ADAPTIVE IMMUNITY: Function of the immune system that is associated with immunologic memory following previous exposure to an antigen, mediated by B and T cell lymphocytes.

ANTIBIOTIC: Institution- or facility-specific data reporting patterns of commonly occurring pathogens and their sensitivity to antibiotic therapy.

ANTIMICROBIAL STEWARDSHIP: A comprehensive program of infection control, surveillance, and judicious antibiotic usage aimed at reducing the development of microbial resistance and optimizing drug therapy outcomes.

ASYMPTOMATIC BACTERIURIA: Presence of two consecutive clean-catch urine specimens resulting in positive cultures (≥100,000 CFU/mL) of the same organism in an individual without any urinary symptoms.

ATYPICAL DISEASE PRESENTATION: Symptoms of illness that do not present in the classic fashion associated with a given disease.

INFLUENZA OUTBREAK: In the long-term care setting, two or more residents of a facility developing respiratory illness within 72 hours of one another, or one laboratory-confirmed case of influenza plus other cases of respiratory infection among residents.
**Fundamentals of Geriatric Pharmacotherapy**

**RECURRENT INFECTION:** The recurrence of infection with an organism other than the organism identified from the previous infection.

**RELAPSE:** Re-emergence of infection with the same organism within 3 weeks after completion of antibiotic drug therapy.

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**Introduction**

Infection is a significant source of morbidity and mortality in elderly patients, and age-related changes in immune function combined with frailty increase the risk of infection and its consequences. Infection risk, diagnosis, and treatment present particular challenges in older patients for many reasons. First, there are several changes in the aging immune system that alter the vulnerability and response to infection. Second, the potential for atypical clinical presentation can result in either under- or over-diagnosis of infection. Third, the pharmacotherapy associated with infection often requires special attention to ensure appropriate drug selection, dose, route, regimen, or duration depending on the population or setting. Finally, the acute and often short-course nature of infections present special health systems challenges for the initiation of follow-up of the care plan for patients who are commonly transferred between multiple care venues and providers. This chapter will focus on general principles of infectious disease in older patients. Specific approaches to infection will be illustrated in three common types of infections: urinary tract infections (UTIs), pneumonia, and influenza. Other types of infections are discussed in the organ system–based chapters of this book.

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**Infection**

*Etiology, Epidemiology, and Clinical Presentation in the Geriatric Population*

Immunosenescence is a term that implies age-related changes in the immune system. Many such changes occur in the immune system with advancing age, and although the degree of change is variable across the geriatric population, in general, changes have been documented in both innate and adaptive immunity.¹

Changes in innate immunity include diminished barrier function of the epithelial cells of the skin, respiratory, and gastrointestinal tracts, and changes in biomarkers such as interleukin-6, interleukin 1β, and tumor necrosis factor-alpha. However, although increases in these biomarkers may predict frailty and mortality among older patients, innate immunity appears less affected by aging than adaptive immunity.²

By contrast, significant age-related changes in lymphocyte population have been documented. In particular, changes in T cells, and to a lesser extent B cells, are a marker of immunosenesence.¹ With aging, the total mass and output of the thymus are reduced.¹ In the bone marrow, the total amount of hematopoietic tissue decreases relative to the amount of adipose tissue,³ and the ability of hematopoietic stem cells to proliferate becomes impaired.⁴ Subsequently, lymphopoiesis is impaired.⁵ T cells are affected in a number of ways. Counts of naive T cells are reduced as compared to those of memory or terminally differentiated effector cells.⁶ In addition, repeated exposures to, and reactivations of, latent pathogens such as cytomegalovirus can affect the number of highly differentiated CD4+ and CD8+ cells.⁷ Because these terminally differentiated cells lack the co-stimulatory molecule CD28, this can result in changes in cellular function, including a decreased ability of T cells to activate, proliferate, or secrete interleukin-2. Meanwhile, this is offset by an increase in cytotoxic or pro-inflammatory markers.¹ This backdrop of low-grade inflammation has been referred to as inflamm-aging.⁸ It has been suggested that increases in interleukins and accumulation of highly differentiated CD8+ T cells may lead to displacement...
or impairment of other lymphocytes, such as CD4+ T cells. Taken altogether, these changes describe an immune system that has accumulated a high degree of specific “learned” immunity in the differentiated memory cells. However, the price paid for this experience is an accumulation of inflammatory markers, such as IL-6, which is a consequence associated with a lifetime of reacting and adapting to stressors such as infection. At the same time, this may also correspond to the potential for decreased ability to produce and activate naive cells against new infection challenges.

The number of B cells does not seem to change significantly with aging but, as with T cells, there are changes in the make-up of the B cell population. Populations of antigen-experienced cells, which develop specifically in response to environmental or autoantigens, are increased relative to naive follicular B cells. Likewise, the make-up of the reservoir of circulating immunoglobulins is more likely to include immunoglobulins that have undergone somatic mutations. By contrast, naive follicular B cells express unmutated antigen receptors, allowing this functional subset of B cells more diversity of specificity. A reduction in the population of naive follicular B cells relative to the more antigen-experienced cells may result in high sensitivity for familiar exposures yet less adaptability to new ones. For this reason, the aging immune system has been described as a “victim of its own success” as populations of naive T and B cells, which are crucial for adaptive immunity, are replaced by encroaching populations of memory T and B cells.

The quality of a patient’s immune response correlates with overall health status. The Frailty Index, which is a measure of health-related deficits, predicts response to vaccination, such as the pneumococcal vaccine, and can be used to evaluate the relationship between health status and T cell activity and other biomarkers of immunologic age. In addition, environmental exposures, comorbid conditions, medications, nutrition, oral health, and institutional infection control measures also influence the degree of vulnerability to infectious diseases. The burden of infection and resulting morbidity and mortality is especially high in the long-term care setting, where an estimated 1.6–3.8 million infections occur in U.S. facilities each year, associated with more than 380,000 deaths and costs estimated between $673 million and $2 billion annually. In addition, the experience of hospitalization due to infection increases the risk of subsequent dementia diagnosis.

The predominant infection types reported in this setting vary from country to country, and reporting rates are influenced by what standards are applied to the confirmation of infection but most commonly involve the urinary tract and the respiratory tract. UTI has been estimated to occur at a rate of 0.1–2.4 cases per 1,000 resident days, the rate for pneumonia has been estimated at 1 case per 1,000 resident days, 10 times the rate of pneumonia among older patients in the community setting. Infection is a common cause of hospital admission, and the rate of hospitalization increases with age. For every 5-year increment over age 65, the rate of hospitalization for influenza or pneumonia increases, and hospital length of stay also increases. Influenza and pneumonia are leading causes of mortality among individuals over age 75. However, mortality risk differs among age strata within the older population. Although 90% of influenza-related deaths occur among individuals over age 65, when this population is stratified into “young old” (<70 years) and “old old” (>85 years), the mortality risk is 16 times higher in the older cohort as compared to the younger.

To combat this, antibiotic drug therapy is a primary line of defense. Antibiotics are the most common class of drugs prescribed in the long-term care facility (LTCF) setting, with 4.8 courses prescribed per 1,000 resident days. Between 47% and 79% of LTCF residents are exposed to at least one course of antibiotic drug therapy during a 1-year period. It is common for antibiotics to be prescribed without microbiological confirmation, yet for infections associated with isolated microorganisms, the
rate of multidrug resistance has been reported to be as high as 24%. In fact, rates of several types of resistant organisms are higher among individuals aged 65 years, including:

- methicillin-resistant *Staphylococcus aureus*,
- vancomycin-resistant enterococci,
- fluoroquinolone-resistant *S. aureus*,
- coagulase-negative *Staphylococcus*,
- Enterococci,
- Viridans group streptococci, and
- Klebsiella with extended spectrum beta lactam phenotypes.

Infection is more severe and mortality risk is higher for facility residents that have infections with these types of resistant organisms, and the cost of their hospital care is higher.

Due to the high rates of susceptibility to infection and subsequent hospitalization and mortality risk among older patients, coupled with the potential for difficult to treat, resistant organisms, there is a strong desire to treat infection aggressively in this population. This is reinforced by the knowledge that, when treating serious infections such as pneumonia, early initiation of antibiotic therapy is associated with lower 30-day mortality. This is complicated, however, by concerns of antibiotic overuse, which exacerbates the risk of antibiotic resistance and increases the risk of adverse effects associated with this drug therapy. Antibiotics have the second highest rate of adverse drug events in the LTCF setting. In addition, overuse of antibiotics increases the risk of development of *C. difficile*–associated diarrhea. Moreover, with the high rate of transfer of patients between healthcare venues, poor infection control and inappropriate antibiotic use patterns in just one facility can easily lead to spread of organisms to adjacent healthcare institutions. This sets up a conundrum for the clinician caring for the older patient: maximizing the aggressive use of antibiotics for the most severe or life-threatening infections while minimizing or avoiding unnecessary or inappropriate antibiotic use.

One of the biggest challenges that prevents appropriate antimicrobial use among frail populations is atypical disease presentation. Older patients often do not exhibit the classic signs and symptoms attributed to infection among the general adult population but instead present atypically. One study of patients over age 75 reported that 27% with a bacteremic UTI did not mount a fever greater than 100.6°F (38°C) and over 48% did not have urinary tract symptoms. Although optimal pharmacotherapy is contingent on many factors, it fundamentally begins with appropriate medication-indication match. Factors that confound or confuse the accuracy of infection diagnosis undermine the appropriateness of antibiotic use. This can result in under-diagnosis, with subsequent failure to treat the infection, or over-diagnosis, which is not only associated with unnecessary antibiotic use but is also associated with the failure to address the true underlying cause of the illness.

**Standard Adult Treatment Recommendations**

In general, the approach to infection in the adult patient involves an assessment of reported symptoms and body temperature. Fever is defined as an increase of at least 2°F (1.1°C) above normal body temperature. Assuming a baseline of 98.6°F (37°C), a body temperature of 100.6°F or greater (>38°C) satisfies this definition. Suspected infection is confirmed, where appropriate, with microbiologic culture or other diagnostic tests such as chest radiograph (CXR). Where microbiologic culture is possible/appropriate, antibiotic therapy is ideally guided by sensitivity analyses. When considering antibiotic drug therapy several considerations apply, including (1) obtaining a thorough medical and medication history, (2) stratifying risk for severe or resistant infections based on patient characteristics, (3) selecting early empiric antibiotic therapy based on national guidelines and tailored to local antibiogram data, (4) dosing antibiotic drug therapy to pharmacokinetic and pharmacodynamics parameters (while still
achieving effective therapeutic concentrations), and (5) de-escalating therapy when possible based on the identified pathogen or the patient’s response as indicated by attainment of goal clinical parameters. Although all of the above are important for all patients with an infectious disease, there are special considerations that present challenges in older or frailer cohorts.

Complete and accurate execution of each of the steps above is crucial to antibiotic stewardship. Effective antibiotic stewardship has been described as a process that ensures that every patient receiving antibiotic therapy is receiving optimal therapy. At the institutional level, this includes initiatives such as observance of environmental and hygiene precautions, implementation of guidelines for antibiotic selection and use, and ongoing surveillance. For individual patients, this also includes accurate assessment and diagnosis, personalized dosage adjustments, and monitoring for regimen adherence and attainment of therapy goals. Various benefits of antimicrobial stewardship that have been reported include a reduction in the emergence of microbial resistance, a decrease in antibiotic complications associated with inappropriate antibiotic use, such as Clostridium difficile infections, and cost savings. It has also been asserted that activities to optimize antibiotic efficacy and minimize adverse outcomes through therapeutic drug monitoring programs or outpatient drug therapy reconciliation/surveillance are not only part of antibiotic stewardship but also constitute patient safety.

**KEY POINT:** A broader definition of fever has been recommended for frail elderly patients.

Although it is recognized that mental status and functional changes are associated with the illness presentation of infection among elderly patients, this is general and somewhat subjective criteria. Standard criteria describing the degree or nature of these changes have not been validated. Therefore, use of the confusion assessment method (CAM) has been suggested as a way to standardize the approach to mental status assessment when infection is suspected. This tool is described in Chapter 12. The CAM criteria have been incorporated into the Minimum Data Set (MDS) 3.0, the tool used by U.S. LTCFs for resident assessment and monitoring. Because the MDS tool also contains a scoring system to evaluate activities of daily living, it has also been suggested that an acute decline in functional status could be documented in a standardized way using these MDS data.
sensitivity and specificity of these criteria for predicting infection, these are measures that are already universally performed in U.S. LTCFs.

Regardless of the suspected infection source, the IDSA recommends that the initial laboratory assessment include a complete blood count (preferably with manual differential), to be performed in conjunction with other diagnostic tests specific to the suspected site of infection. The presence of an elevated white blood cell (WBC) count (WBC count ≥14,000 cells/mm³), a left shift (>6% band neutrophils), or a total band neutrophil count ≥1,500 cells/mm³ is predictive of infection with or without the presence of fever. To avoid failure to recognize alternative or co-presenting illness, the assessment of the patient with suspected infection should include evaluation of the chest (heart rate, respiratory rate, and lung sounds), hydration status, mental status, and physical assessment of the mouth, throat, conjunctiva, skin (including sacral, perineum, and perirectal areas), abdomen, and any indwelling devices.

**KEY POINT:** When adjusting the dose of an antibiotic regimen based on bedside estimates of creatinine clearance, consider keeping the first dose unadjusted for patients with more serious infection.

**Barriers in Treatment of the Geriatric Population**

Distinctions such as community acquired, nosocomial, hospital acquired, and healthcare acquired have evolved over time in an effort to allow a more targeted approach to empiric antibiotic selection. However, even the most current recommendations are based on data from specific types of institutional settings. Even when the type of setting is known, there can still be significant variability. For instance, the term long-term care facility can apply to high-acuity skilled care environments in or adjacent to a hospital, or they may apply to small residential facilities in a community setting. Because older patients are commonly consumers of healthcare services in many environments, it is often difficult to know which criterion is most applicable for determining the suspected organisms. Therefore, where possible, infection surveillance to determine institution-, facility-, or community-specific patterns of causative organisms and susceptibility are necessary for optimal empiric therapy.
Another pitfall involves access to providers and diagnostics, and limits to route of antibiotic administration. Some of the most frail patients in the healthcare system, such as those residing in LTCFs may not have frequent access to a physician or diagnostic tests. In this environment, the IDSA recommends that the initial assessment be performed by a certified nursing assistant, who reports findings to the charge nurse, who in turn communicates with a provider (a physician or midlevel practitioner) who is remote to the site of care. Orders for diagnostic evaluation or drug therapy are usually made by phone or electronic transmission. Given the potential for atypical disease presentation, it is essential that a thorough assessment be performed, which is beyond the capabilities of a certified nursing assistant (CNA). Although there are no published studies that differentiate resident outcomes based on the type of provider performing the assessment, a care model where initial assessment data are reported via telephone to a provider who is remote to the site of care provides few safeguards against incorrect diagnosis if the report does not include complete data. Therefore, each individual must be optimally trained to perform the assessments appropriate to his or her respective scope of practice, both to recognize infection and to exclude other possible causes of the illness presentation. Breakdowns and shortcuts in this chain of reporting may be responsible for inappropriate diagnosis or treatment.

This potential for misinterpretation of disease presentation is especially problematic if the diagnosis is made without the confirmation of diagnostic testing. Residents of facilities associated with a hospital will usually have access to rapid and convenient laboratory or diagnostic testing; however, community-based facilities must either contract with external vendors for clinical laboratory and mobile radiology services or arrange transportation to diagnostic facilities. Sometimes a patient cannot or will not tolerate or cooperate with the trip or the procedure, or advance directives expressly prohibit transfer. In such situations, the choice is sometimes made to forego diagnostic testing, and an antibiotic is initiated in the absence of diagnostic confirmation, heightening the need for optimal clinical assessment.

The logistical barriers described above, in addition to the potential for misdiagnosis due to atypical disease presentation, are variables that potentially erode antibiotic stewardship practices. There are limited data describing stewardship in the long-term care setting despite the prevalence of antibiotic use and drug resistance in this environment. However, one study described perceptions and attitudes of various healthcare providers in the long-term care setting toward antibiotic stewardship and identified several themes. Among the population studied, most staff members did not believe current antibiotic use was excessive, and prescribers admitted to “just in case” prescribing, citing pressure from facility staff or patient family members as the most significant impetus for unnecessary prescribing. In addition, many prescribers stated they had not encountered drug resistance but also acknowledged that culture data were often not requested. Although about 50% of prescribers cited emerging resistance as a problem, only a few staff members believed this to be specific to long-term care, citing this as a hospital issue. Most general practitioners and pharmacists surveyed believed that antibiotic resistance was a problem associated with inappropriate antibiotic prescribing. Specifically, pharmacists highlighted inappropriate antibiotic durations and lack of specified end dates as a particular problem. By contrast, most nurses believed resistance to be a problem of poor infection control practices. With respect to attitudes toward the potential success of stewardship interventions, most general practitioners cited hindrance of prescriber autonomy as the biggest potential barrier. Among facility staff, most nurse managers cited potential lack of acceptance of stewardship protocols by staff members due to workload, yet staff members cited concerns about physician acceptance of interventions as the most significant barrier. The off-site nature of prescribers and pharmacists was also cited as a logistical barrier.
**Urinary Tract Infection**

**Etiology, Epidemiology, and Clinical Presentation in the Geriatric Population**

UTI is one of the most common types of infection among elderly patients, with up to 10% of older adults experiencing a symptomatic UTI each year, and it is the most frequent reason for exposure to antibiotic drug therapy among residents of LTCFs. The prevalence of UTI increases with age in both men and women but is more common among female patients at a rate of two to one in the elderly. In both sexes, UTIs can occur in the bladder (cystitis), the urethra (urethritis), or the kidney (pyelonephritis). In men, another concern is prostatitis, which can be mistaken for simple UTI. In addition to previously discussed age-related risk factors for infection, risk factors for UTI include structural or functional abnormalities of the urinary tract, declining renal function, incontinence, and catheter use. Postmenopausal vaginal changes such as atrophic vaginitis can mimic UTI symptoms among women, as can history of UTI during menopause and presence of a cystocele. Among men, benign prostatic hyperplasia can result in urinary symptoms, including postvoid residuals, which increase the risk of bacterial colonization and infection. Among institutionalized older adults, catheterization, incontinence, antimicrobial exposure, and functional status are the most common predisposing factors associated with recurrent UTI.

**Symptom Presentation and UTI Diagnosis**

General symptoms typically include fever, dysuria, urinary frequency, or flank pain; however, older patients may present atypically. One criterion that is often applied to identify UTI is the McGeer criteria, in which three of the following conditions must be met for a suspected UTI:

- Fever (>38°C) or chills
- New or increased burning sensation on urination
- New flank pain or suprapubic tenderness
- Changes in urine properties, such as dark color or foul odor
- Mental function decline

These criteria are modified for individuals with an indwelling catheter as follows: the criterion “changes in urine properties” is omitted from the list of conditions, and patients must meet two of the remaining four criteria. It is also important to remember that although a dark color or foul odor can be suggestive of UTI, other factors can alter urine character, including dehydration, renal impairment, bleeding, and drug therapy, so these signs alone are not reliable for diagnosing UTI.

Traditionally, once these criteria have been met, the performance of a urinalysis has been recommended. In noncatheterized symptomatic individuals, a quantitative count of ≥10⁵ CFU/mL of an organism in a single specimen is usually considered diagnostic of UTI. This threshold is lower, ≥10³ CFU/mL of a single predominant pathogen, among catheterized individuals. The most common organisms associated with UTIs are summarized in Table 17-1.

Other factors that are also considered in the identification of UTI are presence of pyuria and nitrite on urinalysis. Although pyuria is usually present with symptomatic UTI, in elderly long-term care residents, 90% of asymptomatic individuals and 30% of individuals without bacteriuria have pyuria. This may be because of other causes of bladder, genital, prostate, or renal inflammation, and when present pyuria cannot distinguish symptomatic from asymptomatic bacteriuria. By contrast, the absence of pyuria has 100% negative predictive value for UTI, making it possible to rule out UTI when this finding is absent. Urinary nitrite is a sign that suggests a byproduct of bacterial metabolism. However, not all bacteria produce nitrites. Even in combination, positive pyuria and nitrite in a urinalysis have only 80% predictive value for UTI, a value that is reasonably reliable but for the need to practice good antibiotic stewardship. These factors should not be considered alone in the diagnosis of UTI.
<table>
<thead>
<tr>
<th>Infection Type</th>
<th>Common Causative Organisms</th>
<th>Antibiotic Therapy Options</th>
</tr>
</thead>
</table>
| **UTI**        | *E. coli* (most common in women)  
*P. mirabilis* (most common in men)  
*K. pneumonia*  
*Citrobacter* spp.  
*Enterobacter* spp.  
*Providencia* spp.  
*M. morganii*  
*P. aeruginosa*  
*S. aureus*  
*Enterococcus* spp.  
Coagulase-negative staphylococci  
Group B streptococci | Oral:  
Trimethoprim/sulfamethoxazole; trimethoprim; cephalosporins; amoxicillin/clavulanate; fluoroquinolones; nitrofurantoina  
Intravenous:  
Ampicillin; third-generation cephalosporin; gentamicin; tobramycin; fluoroquinolone+ (+IV usually only necessary if patient cannot take oral medication) |
| **Pneumonia** | Non-intubated:  
*S. pneumonia*  
*H. influenza*  
*M. catarrhalis*  
*C. pneumonia*  
*K. pneumonia*  
*M. pneumonia*  
*S. aureus*  
Gram-negative bacilli: viruses  
Ventilator associated:  
*S. aureus*  
Gram-negative bacilli:  
*S. pneumonia*  
*P. aeruginosa*  
Anaerobes +/- bacteria listed above | Levofloxacin or moxifloxacin; amoxicillin/clavulanate plus macrolide; ceftriaxone or cefotaxime plus macrolide; ampicillin/sulbactam plus macrolide  
Cefepime or ceftazidime; piperacillin/tazobactam plus ciprofloxacin plus vancomycin; imipenem or meropenem  
Piperacillin/tazobactam plus ciprofloxacin plus vancomycin; or clindamycin or metronidazole plus: cefepime or ceftazidime or imipenem or meropenem |

*aOnly for Creatinine Clearance (CrCl) >60 mL/min.  
IV, intravenous.*
Once diagnosed, a UTI is categorized based on the suspected site of infection (upper or lower urinary tract) and classified as either complicated or uncomplicated to guide therapy. Most symptomatic UTIs are classified as complicated in the elderly. Male patients, especially those who present with either relapsing or recurrent infection, should also be evaluated for possible prostatitis, as this requires different drug therapy than UTI.

Asymptomatic Bacteriuria

An important, and potentially confusing, concept when discussing UTI among older patients is asymptomatic bacteriuria (ASB). The urinary tract is usually sterile, except for the distal urethra, but ASB occurs when bacteria colonize the urethra or bladder and possibly enter the kidneys. It is officially defined as the presence of two consecutive clean-catch urine specimens resulting in positive cultures (≥100,000 CFU/mL) of the same organism in an individual without any urinary symptoms. The definition has been recently modified to allow the identification of ASB for a single clean-catch specimen for men, to establish a lower colony count threshold for catheterized individuals, and to clarify that pyuria is not a factor that meets the criteria for symptomatic bacteriuria.

The prevalence of ASB increases with age and level of frailty, with the prevalence approaching 20% among community dwelling individuals over age 70 years and up to 40% to 50% in LTCFs. In the absence of genito-urinary localization of symptoms, bacteriuria should not be treated. Therefore, because of the high likelihood that a urine sample will yield a positive culture anyway, routine screening for ASB is not recommended unless a patient will be undergoing transurethral resection of the prostate (in men) or other urologic procedures where mucosal bleeding is anticipated.

Standard Adult Treatment Recommendations

Initial Treatment

The goals of UTI treatment include eradication of the causative organism, prevention of consequences of infection, including bacteremia or other more serious infection, and prevention of relapse or recurrence of infection. Based on the most likely suspected organisms, the antibiotic drug therapies usually employed to treat UTI are listed in Table 17-1. Once the antibiotic drug therapy has been selected, duration of therapy must be considered. A determination of uncomplicated versus complicated UTI is used in determining the duration of therapy. Short-course therapy of 1, 3, or 5 days duration has been studied in young women with uncomplicated infection. Other treatment regimens in women are typically 7–10 days for women and 10–14 days for men. However, if a male patient is diagnosed with prostatitis, treatment durations should last 4 weeks for an acute infection and 12 weeks for chronic infections.

Prevention, Recurrence, and Relapse

There are several strategies that are often used to prevent UTI, some of the most important of which are nonpharmacological infection control precautions such as hand washing and other institutional or environmental safeguards. Two common dietary supplements used in prevention are cranberry and vitamin C. It has been reported that cranberries or cranberry juice exert antibacterial activity by preventing bacterial adherence to the lining of the urinary tract, specifically via the proanthocyanidin compound. Despite this putative mechanism, clinical literature evaluating the effectiveness of cranberry has been mixed. Unfortunately, the reliability of the data is often plagued by poor study design or lack of power. In addition, not all juices and dosage forms contain a uniform amount of the active compound. Ascorbic acid (vitamin C) has been
used in chronic and recurrent UTIs. It is thought to acidify urine and thus prevent proliferation of bacteria. However, at usual doses, urinary acidification is minimal and data supporting a prevention benefit are insufficient. The use of ascorbic acid is discouraged because it is metabolized to oxalic acid, and, therefore, high-dose vitamin C is associated with development of calcium oxalate stones. A prophylaxis regimen may be considered when recurrent infection is suspected. Recurrent infection is described as the recurrence of infection with an organism other than the organism identified from the previous infection. The choice of prophylaxis is based on the frequency of recurrence. Although different definitions of recurrence exist, including two infections within 6 months or three infections in 12 months, a threshold of three or more infections in the span of 1 year is often considered as a criterion for prophylaxis. Data among young women in an ambulatory care setting with more than three UTIs per year suggest that prophylactic therapy may decrease recurrences. Regimens typically employed include trimethoprim-sulfamethoxazole, nitrofurantoin, and cephalexin, although resistance rates affect the utility. Another agent, methenamine, has Food and Drug Administration (FDA) approval for UTI prophylaxis. It is used as a urinary antiseptic, usually in combination with vitamin C. However, this therapy is poorly tolerated because of gastrointestinal side effects and must be used with caution in renal impairment. Its efficacy is questionable for organisms such as proteus, Enterobacter sp, or P. aeruginosa.

It is important to distinguish recurrent infection from relapsing infection. Relapse refers to a persistent infection with the same organism after completion of antibiotic drug therapy for UTI. A variety of factors may result in this therapeutic failure. It could indicate the selection or dose of the antibiotic was suboptimal, or the duration of therapy was inadequate—especially if the infection was more complicated, involving the kidney, prostate, or complicated by a structural abnormality of the urinary tract. Alternatively, it may be possible recurring symptoms are due to an unrelated medical condition for which the differential diagnosis is clouded by the presence of a chronic bacteriuria. Additional diagnostic evaluation to rule out other possible conditions or urological evaluation to dismiss structural abnormality may be necessary.

### Treatment Recommendations in the Geriatric Population

Few high-quality data exist to provide criteria for diagnosis and treatment of UTIs in long-term care settings. The McGreer criteria, although routinely used in a variety of settings, have not been validated in all settings and have not been updated in many years. Several concerns have been cited regarding its use among frail patients:

- When a true febrile response is difficult to evaluate or self-report of symptoms is not reliable, and when common comorbid conditions such as dehydration or drug therapy can result in fever, concentrated odiferous urine, or confusion, it is easy to postulate scenarios in which a patient may satisfy multiple criteria from the McGreer list yet actually have another underlying problem.

- When illness presentation is atypical, there is also temptation to stretch the application of the McGreer criteria to include other nonspecific symptoms of clinical deterioration, although studies have not supported this and the McGreer criteria do not specifically endorse this.

As a result, various infection control organizations and consensus groups provide recommendations to assist with the diagnosis of UTIs and optimize antibiotic utilization. In particular, the IDSA has published guidance endorsed by the American Geriatrics Society regarding infection in the long-term care setting. Another widely cited criteria are the Loeb criteria. Some of the new considerations that have been suggested to modify or add to the original McGreer criteria include:
• adding a complete blood count (CBC) to evaluate WBC count as a method to further distinguish infection from other causes;22
• modifying the threshold for fever to align with the 2008 IDSA criteria;
• specifying the criteria for mental or functional status change to state “acute change in mental status or acute functional decline with no alternate diagnosis and leukocytosis”; and
• clarifying the criteria for “acute dysuria” to include localizing genitourinary findings.23,58

Taken all together, fever or leukocytosis plus one localizing UTI symptom, or the presence of two or more new or worsening localizing UTI symptoms, could meet the definition for symptomatic UTI.23

The inclusion of serum chemistry assessments in the UTI evaluation can be a useful addition to the patient assessment. This is, in part, because it can provide data regarding conditions that can mimic UTI, such as dehydration, and also because it can provide current data on which to base an estimate of creatinine clearance, which may be necessary if an antibiotic or other drug therapy is to be prescribed.22,44

The importance of the suggested modifications becomes apparent when considering the risk of inappropriate prescribing for asymptomatic bacteriuria. None of the criteria recommends treatment for this condition; however, it can be difficult to distinguish the patient who is truly asymptomatic for UTI.22 A patient presenting with atypical symptoms of almost any condition is not “asymptomatic”; therefore, if a premature assumption is made regarding UTI as the causative problem, previous criteria that rely on assessment of urinalysis and culture as the primary diagnostic evaluation do not provide a safeguard in the event another condition besides UTI is responsible for the presentation. Given the high prevalence of bacterial colonization among elderly patients, especially in long-term care, it is likely the urinalysis and culture will yield bacterial growth. However, this finding may not be specific to the actual underlying illness. Admittedly, extra diagnostic tests, even relatively noninvasive ones, result in increased cost. Additional data are needed to critically evaluate the overall cost benefit and potential for unnecessary antibiotic avoidance associated with this enhanced diagnostic approach.

Drug Therapy Selection and Use
The suspected causative organisms for UTI among older patients are generally similar to those identified in younger populations. More so than age, living environment is more likely to influence the risk of exposure to certain organisms. For instance, Providencia sp. is predominantly identified in the long-term care setting. However, age- and disease-related physiological changes do influence the way antibiotics are used.59 If empiric antibiotic therapy is initiated, previous urine cultures from the patient and, if applicable, endemic institutional pathogens should be considered when choosing an agent.51 The superiority of any one particular antimicrobial agent as empiric therapy, in either efficacy or adverse effects, has not been demonstrated. This is due to a variety of factors, including limited comparative data, heterogeneity of study populations (including enrollment of both genders and asymptomatic versus symptomatic patients), and limitations of sample size and follow-up.53

Careful attention must be paid to appropriate dose. There is an increased potential for adverse effects demonstrated in the context of comorbid dementia, dehydration, or renal impairment, especially when renal dose adjustments do not occur.58 Many antibiotics carry recommendations for dose adjustment based on estimated creatinine clearance (CrCl), but of special note is the recommendation to avoid the use of nitrofurantoin when glomerular filtration rate is <50 mL/min. Although most dose adjustment recommendations are aimed at reducing an excessive dose, this is a recommendation to avoid the use of potentially ineffective therapy, as nitrofurantoin must be filtered via the kidney to reach its site of action in the bladder.60 Another age-related safety recommendation for
antibiotic therapy involves fluoroquinolones, which have been cited in a recent FDA advisory warning about an increase of tendonitis and tendon rupture in adults over age 60.61

In most cases, older adults do not meet the requirements for short-course therapy. Among older adults, UTIs are usually considered to be complicated, especially among male patients.53 Moreover, atypical symptom presentation clouds the ability to differentiate uncomplicated from complicated infection. Therefore, because elderly individuals are not well represented in clinical trials of short-term courses of antibiotic drug regimens (such as 3-day therapy), the likelihood of efficacy for short-course therapy cannot be reliably predicted.55 One study of elderly women in both nursing home and community settings showed that 98% of the individuals in the nursing facility setting received at least 7 days of therapy compared to 77% of the community subjects, and the nursing facility patients were five times more likely to have at least 10 days of therapy. The frequency of both infection relapses and drug side effects was higher in the nursing home group.62 Therefore, data are inconclusive regarding an established duration of therapy that is appropriate for older adults. Most empiric recommendations suggest durations of at least 7–10 days, with longer courses of therapy in circumstances where known complications exist, such as structural bladder abnormality (10–14 days) or pyelonephritis (14–21 days).44,51 Once the course of treatment has been completed, there is no evidence to recommend repeated urine cultures to document cure unless problematic symptoms persist.51

**Prevention, Recurrence, and Relapse**

With respect to UTI prophylaxis among frail populations, the risk of recurrent infection must be weighed against safety concerns associated with long-term antibiotic use, including bacterial resistance and C. difficile–associated diarrhea. This is especially of concern in long-term care settings, where prescribers employing recurrent or chronic courses of antibiotic therapy for individual patients are often external to the care environment, and individual antibiotic utilization patterns may or may not be coordinated with internal facility protocols for infection control. The importance of institutional infection control protocols is well described, but when they are not optimally employed it is not clear that chronic antibiotic therapy is an appropriate intervention.17,63 Until definitive studies are conducted to better identify criteria for appropriate use of antimicrobial prophylaxis in UTIs, this practice should be discouraged in this setting.56,57 Instead, nonpharmacological prevention of UTIs in older adults should always be employed in all settings, including basic infection control practices such as hand washing.56 Elderly women who perform their own personal hygiene should be reminded to wipe from front to back after a bowel movement or urinating. Caregivers both at home and in the long-term care facility must assist with this if necessary. If an individual is incapable of performing the personal care practices that prevent the recurrence of UTIs, then it becomes a larger burden on the part of the caregivers.56

Finally, there is evidence among postmenopausal women that intravaginal administration of estrogen cream is associated with prevention of recurrent UTI.64 This strategy is based on the premise that estrogen deficiency can result in alteration of vaginal bacterial flora and subsequent increase in colonization of E. coli.56,64 The optimal duration of this therapy is not known and because of the risks associated with estrogen use, even in low dose topical forms, the true balance of risk-benefit associated with chronic UTI prophylaxis has not been established.

**Special Consideration: Catheters**

Up to 10% of residents in long-term care settings have chronic indwelling catheters, which are associated with an 80% to 95% chance of bacteriuria occurring within 30 days of catheterization, and this colonization is common with multiple organisms.44,54 This bacteriuria may be prevented by avoiding use of a chronic indwelling catheter, if at all possible, or limiting its duration. Use of a closed drainage system may decrease risk...
of infection in the short term, but with chronic use the prevalence of bacteriuria approaches 100%; in fact, bacterial colonization occurs within 30 days for 80% to 95% of patients and is commonly polymicrobial in nature. Routine irrigation of catheters does not lower rates of symptomatic UTI or catheter obstruction. Systemic antibiotics can temporarily eradicate the presence of bacteria, but re-infection can occur and a subsequent resistant organism may result from this practice. Therefore, a compelling need exists to ensure that antibiotic therapy is limited to true infection. This need is offset by a concern that placement, removal/replacement, or trauma associated with the catheter is a common cause of bacteremia from a urinary source. Previous criteria for identifying UTI for a catheterized individual employed a lower bacterial colony count and required fewer items from the McGeer criteria, which may result in earlier antibiotic intervention for individuals at risk for very serious infections. However, it is not clear how this is balanced by any increase in risk for exposure to an unnecessary antibiotic, and it has been recommended that a threshold colony count of >10⁵ CFU/mL be employed for all individuals regardless of the presence of an indwelling catheter for the diagnosis of symptomatic UTI. Among catheterized individuals, the Loeb criteria suggest minimum criteria that must be met to support a diagnosis of UTI, which include fever, new costovertebral tenderness, rigors, or new onset delirium. Drug therapy selection in patients with catheters is similar to that in individuals without a catheter. The optimal duration of therapy is not known, but in the absence of evidence-based recommendations, many clinicians simply treat this as a complicated infection with a minimum of 7 days treatment as the standard practice.

Barriers in Treatment of the Geriatric Population
A medication review may be needed to identify drug-induced causes of urinary complaints. Medications that increase urinary frequency, such as diuretics or cholinesterase inhibitors, can increase UTI risk if this side effect is not managed with diligent personal hygiene for incontinent episodes. In contrast, medications that worsen urinary retention, such as narcotic analgesics, sedatives, and anticholinergic medications, can also increase risk of UTIs by contributing to post-void residual. Elderly patients, especially men with benign prostatic hyperplasia, are especially sensitive to the effects of anticholinergics. In either case, symptoms can be assumed to be dysuria and attributed to UTI. The need to screen for and consider the contribution of these side effects becomes compelling, especially among patients who are identified as having recurrent UTI.

Pneumonia
Etiology, Epidemiology, and Clinical Presentation in the Geriatric Population
Pneumonia and influenza together make up the eighth leading cause of death from any cause and the first cause of death from infection in the elderly population in the United States. In addition to previously discussed risk factors for infection, specific factors related to the respiratory tract that increase vulnerability to pneumonia include decreased reserve capacity in the lungs, reduced respiratory muscle endurance, slowed mucociliary transport, and reduced ability to expectorate and clear bacteria. Comorbid conditions that increase pneumonia risk include chronic obstructive pulmonary disease (COPD), heart disease, diabetes, malignancy, hepatic disease, malnutrition, dysphagia, neurological disorders, prior antibiotic therapy, poor quality of life, immobility, cigarette smoking, and use of medications that can interfere with immune response (e.g., corticosteroids). The suspected causative organisms can vary based on context. In general, in all care settings the most commonly identified organism among elderly patients with pneumonia is S. pneumoniae. However, it can often be difficult
to obtain adequate sputum cultures, so that in more than 50% of cases the causative organism is unknown. Transient bacterial colonization of the oropharynx with organisms such as S. aureus, K. pneumoniae, and E. coli is common in the elderly population. Gram-negative colonization may be likely among patients who are immobile or who have cardiopulmonary comorbidities. Although P. aeruginosa and gram-negative enteric bacilli are not typically associated with community-acquired pneumonia, recent hospitalization or other exposure to a healthcare environment, aspiration, prior antibiotic therapy, or pulmonary comorbidities have a higher risk for infection with these organisms. Individuals with dysphagia are vulnerable to aspiration pneumonia, which is likely to be polymicrobial in nature. Aspiration pneumonia has often been associated with anaerobic infection as well, but functional risk factors have been identified that suggest which dysphagia patients are most likely to experience infection due to anaerobic organisms, as discussed in Chapter 11. Atypical pathogens (such as C. pneumoniae) have been found to cause a higher frequency of infection in patients age 65–79 than in patients 18–39 and spread particularly in communal living environments such as long-term care. Finally, the incidence of drug-resistant S. pneumoniae (DRSP) is rising among elderly patients, especially patients with a history of prior antibiotic therapy, alcoholism, immune suppression, and multiple comorbidities.

Fever and cough are two of the most easily recognized signs of pneumonia in the general adult population, and most older patients with pneumonia are still likely to present with these classic symptoms. In fact, one study reported that among older patients with CXR-confirmed pneumonia, almost half had a temperature greater than 100.4°F (38°C) and over 90% had respiratory symptoms. Still, atypical presentation may be confusing and delay diagnosis and treatment for older patients. Nonspecific presentations can include confusion, weakness, lethargy, failure to thrive, change in mental status, falls, and general clinical decline, and these can easily be misattributed to other chronic conditions. In addition, chronic conditions such as COPD, heart failure, or diabetes can mask the presence of an infection, and the decompensation of one of these conditions should actually be considered as a possible first sign of pneumonia. Additional signs that have good predictive value for both pneumonia diagnosis as well as risk of 30-day mortality among older patients include tachypnea, as defined by a respiratory rate of at least 25–30, and oxygen saturation less than 90%.

In all patients with suspected pneumonia, the gold standard for diagnosis is a CXR for both identifying the presence of pneumonia and determining its severity. Sputum gram stain and culture (before antibiotic therapy) can also be helpful but is only useful if a patient can produce a quality specimen. Older patients may lack the expiratory force to cough up adequate sputum, and bronchial lavage is not routinely employed to obtain a sample. Most clinical laboratories will reject samples with a high count of squamous epithelial cells, an indicator that the sample is more saliva than sputum. Blood cultures are usually only recommended for severely ill patients in whom bacteremia is suspected. In situations where a CXR is not feasible or when patient directives preclude transfer to a hospital or diagnostic environment, scoring systems have been devised to estimate the likelihood of a pneumonia diagnosis in the absence of radiographic confirmation. Factors supporting diagnosis include elevated WBC count, respiratory rate >30 breaths per minute, the presence of somnolence and acute confusion, lung sounds such as wheezes or crackles, and heart rate greater than 110 beats per minute.

**Standard Adult Treatment Recommendations**

The IDSA and the American Thoracic Society (IDSA/ATS) have developed guidelines for the treatment of pneumonia. The recommended empiric treatment will vary depending on the clinical setting and the patient’s comorbidities and risk factors but should cover the common
pathogens in Table 17-1. If the causative pathogen can be determined, therapy should be tailored based on culture and sensitivity results.

After therapy has been initiated and response has been determined, guidelines recommend a minimum of 5 days of therapy and that patients remain afebrile for at least 48–72 hours before stopping therapy.35 For those patients receiving intravenous therapy, a switch to oral therapy can be considered when the patient is clinically stable. Oral treatment is indicated with improvement in cough, sputum production, dyspnea, fever (afebrile on two separate occasions 8 hours apart), WBC count, and ability to tolerate oral medications.68,78

Treatment Recommendations in the Geriatric Population

Due to the high risk of mortality associated with pneumonia in the older population, timely administration of antibiotic is crucial.76 Although the most likely pathogen as well as local resistance patterns should be considered when selecting empiric therapy, a respiratory fluoroquinolone or a macrolide plus a beta-lactam is the generally recommended empiric therapy for elderly patients, whether as outpatients or admitted to the hospital.74,78 Both cover the large majority of pathogens (including DRSP). Although quinolones carry warnings regarding central nervous system side effects, QT prolongation, and tendon rupture, this class of medication remains an attractive option because of its similar bioavailability between oral and intravenous formulations, a consideration that is particularly important in settings where intravenous treatment is not an option. Monotherapy with a macrolide is not recommended for elderly patients with comorbidities (liver or renal disease, heart failure, diabetes, malignancy, asplenia, immunosuppressant condition, or on immunosuppressant drugs) or at significant risk for DRSP, especially in areas of known macrolide-resistant S. pneumoniae.74,78 However, a recent study of azithromycin did provide some additional information regarding risk-benefit among older patients with community-acquired pneumonia.79 Previous data had suggested the potential for increased risk of cardiovascular events (specifically QT prolongation and dysrhythmia) and mortality associated with 5-day courses of azithromycin compared to nonantibiotic users or use of amoxicillin.80 However, in a retrospective cohort study evaluating the treatment of community-acquired pneumonia among patients over age 65 for a 10-year period at VA hospitals, regimens containing azithromycin were associated with a lower 90-day mortality (OR 0.73; 95% CI, 0.70–0.76). There was a smaller but significant increase in the risk of myocardial infarction (OR, 1.17; 95% CI, 1.08–1.25) but not for any other cardiovascular event, including dysrhythmia, resulting in a net benefit associated with azithromycin for this population.79

Modification to empiric therapy is considered when P. aeruginosa, methicillin-resistant S. aureus (MRSA), or anaerobic aspiration pneumonia is suspected. Risk factors for P. aeruginosa infection include severe COPD, use of oral corticosteroids, alcoholism, and recent antibiotic therapy. If P. aeruginosa is suspected, an antipseudomonal beta-lactam should be considered. If anaerobic infection is suspected, clindamycin plus a fluoroquinolone is preferred (an alternative being a beta-lactam/beta-lactamase combination).74,77

Historically, pneumonia due to aspiration has been considered a factor for which anaerobic coverage was indicated. However, one investigation determined that lack of anaerobic coverage for elderly patients with aspiration pneumonia was not associated with a poorer outcome, even when anaerobic organisms had been identified via culture.81 Risk factors have been suggested to indicate those individuals for whom anaerobic coverage is most relevant, including functional status (activities of daily living [ADL] score), the presence of chronic underlying respiratory conditions, and whether an enteral feeding tube is present.81,82 These variables may suggest a higher prevalence
of anaerobic to aerobic organisms, as well as Enterobacteriaceae, P. aeruginosa, and drug-resistant organisms, allowing more aggressive therapy to be directed at these targets for patients with such risk factors.83

Several factors influence the success of antibiotic drug therapy among older patients. Utilizing IDSA/ATS consensus recommendations and employing data about local resistance patterns to create guideline-based protocols has been shown to reduce mortality in several studies across the general population.78 However, to evaluate whether this translates to a benefit in treatment outcomes, including length of stay, readmission, or mortality among elderly populations, a study of 17,728 patients from a Utah Medicaid and Medicare database was conducted.84 Guideline compliance was associated with a significant decrease in 30-day readmission rate (OR 0.86; CI 0.78–0.96) and mortality (OR 0.92; CI 0.87–0.98) among patients over age 65 (mean age 72 +/– 12 years) with a diagnosis of pneumonia.84 Additionally, guideline-based therapy is most successful when initiated as soon as possible, ideally within 4–8 hours of arrival to the hospital.36,37

Supportive care of sepsis and septic shock, respiratory failure, and other exacerbations of comorbidities are important for improving outcomes in elderly patients.68,78 Treatment for sepsis and septic shock does not significantly differ for elderly patients with pneumonia than for those with other infections. Noninvasive ventilation with bilevel positive airway pressure or continuous positive airway pressure may be appropriate in patients with underlying COPD or who are in respiratory distress. Prophylactic therapy for deep venous thrombosis should be considered, as elderly patients with pneumonia are at high risk for thrombosis.78 All individuals over the age of 50 should be vaccinated yearly for influenza, and elderly patients ≥65 years should receive the pneumococcal vaccine. Specific vaccination recommendations are discussed in Chapter 16.

### Barriers in Treatment of the Geriatric Population

Similar concerns for classifying infection types and risk discussed for UTI apply to pneumonia. Not only is care needed when basing empiric therapy on community-acquired versus healthcare-acquired designations, it is also important to perform severity assessment to stratify risk. Two tools employed for this purpose are the Pneumonia Severity Index (PSI) and the British Thoracic Society, known as CURB-65. However, although both of these tools have been validated in the adult population, they lack validation in the elderly population.33,43

A potential limitation of the PSI is that it relies heavily on age and comorbidities. This may oversimplify the decision of who should be admitted to the hospital with pneumonia, because most elderly patients with fever would be assessed at least as class III, regardless of functional status.78 In contrast, CURB-65 does not include direct assessment of comorbidities. Instead of endorsing a particular tool, the IDSA/ATS recommends that additional factors not encompassed in clinical decision support tools be taken into account when selecting the appropriate care venue for the elderly.74,77 Such subjective factors include:

- ability to reliably take oral medications,
- outpatient resources (i.e., caregivers for dependent patients),
- access to intravenous therapy,
- uncompensation of comorbidities (i.e., COPD, heart failure, diabetes mellitus, or renal insufficiency),
- psychosocial needs or other medical conditions requiring hospitalization, and
- treatment failure or lack of response to previous empiric therapy.

Another logistical problem that must be considered involves how duration of therapy is determined. In inpatient settings, it is common for clinical criteria to be employed to determine
length of therapy. For instance, criteria such as resolution of fever, WBC count, stability of vitals or mental status, and ability to tolerate oral intake are used to make decisions about switches from intravenous to oral medication, hospital discharge, and discontinuation date of the antibiotic regimen. However, in the outpatient setting, empiric courses of 5 or 10 days are often employed. The empiric method of the outpatient setting is the more common method employed in long-term care settings, and this may be associated with the off-site nature of both the prescriber and the pharmacy vendor. However, given the 24-hour monitoring of a nursing facility, it could be possible for clinical criteria to be used to tailor antibiotic durations in this environment. In addition, for patients moving from one care venue to another it is not sufficient for medication reconciliation forms to include just the name and regimen of the antibiotic. The intent for antibiotic duration must be clearly documented. Strategies to tailor antibiotic duration may represent an area for antibiotic stewardship in two ways. First, it may reduce unnecessary use by curbing excessive duration of therapy. Second, it may avoid subtherapeutic treatment and therapeutic failure by ensuring adequate completion of therapy.

**Influenza**

**Etiology, Epidemiology, and Clinical Presentation in the Geriatric Population**

Influenza is a worldwide contagion. Each year, seasonal influenza causes a broad range of illness ranging from mild fever and chills to severe complications such as pneumonia. Although it has an accepted vaccine to protect against infection, the rate of vaccination in individuals older than 65 has become stagnant in the past decade. The highest rates of death (some estimate up to 90%) from seasonal influenza are individuals aged 65 and older, specifically those with comorbidities and in LTCFs where outbreaks are common.85 H1N1 outbreaks in 2009 showed that rates of illness among those 65 and older were lower than those of other age groups. The risk of infection with H1N1 among individuals older than 65 is less than the risk of seasonal influenza infection. However, although the illness is less frequent among older adults, outbreaks in LTCFs were still reported. It is assumed that these outbreaks resulted from the virus being introduced to the facility by staff or visitors who were infected.86

**Standard Adult Treatment Recommendations**

Treatment commonly depends on the symptoms experienced by the patient. Cough and fever are the most common predictive features of influenza in adults.87 The best treatment for influenza is prevention. Vaccination for seasonal influenza has been shown to reduce the rate of influenza-like illness as well as reduce hospitalization for pneumonia and influenza and has shown a decrease in all-cause mortality.88 The recommended drugs for the treatment of influenza are neuraminidase inhibitors oseltamivir and zanamivir. Amantadine and rimantadine are no longer recommended because of resistance among some influenza A viruses. Neuraminidase inhibitors reduce symptom duration, complications, and hospitalizations among outpatient adults infected with influenza. Oseltamivir is available as a pill and a suspension. The recommended dose is 75 mg by mouth twice daily for treatment. For prophylaxis, oseltamivir 75 mg by mouth once daily is recommended. Zanamivir is an inhaled powder. The recommended treatment dose is 10 mg (two inhalations) twice daily for treatment and 10 mg once daily for prophylaxis. Treatment duration and length of prophylaxis are identical to oseltamivir.

**Treatment Recommendations in the Geriatric Population**

Symptoms of influenza may present differently in the geriatric population. Severe fatigue is usually present at the start of symptoms and can be accompanied by cough, sore throat, nasal congestion, headache, chills, and severe body
aches. Fever may be present but difficult to detect in some older patients. Some individuals may present with nausea and vomiting or dehydration. Others may present with what appears to be complications or worsening of asthma, emphysema, or heart failure. Care should be taken by LTCFs to identify patients exhibiting worsening of symptoms of these diseases during flu season or during an influenza outbreak in the community. Altered mental status has also been reported during influenza infection.

Two seasonal influenza vaccines are available: the regular and the high-dose vaccine. The high-dose vaccine is thought to induce a stronger immune response in individuals older than 65, whose immune systems are weakening. Because the influenza vaccine may have lower effectiveness for older adults, it is imperative not only that they are vaccinated but that their caregivers and close contacts receive the vaccine to reduce the likelihood of their elders being exposed. The high-dose trivalent influenza vaccine is not associated with an increase in adverse effects compared to the standard dose and has shown higher titer levels than the standard dose postvaccination in those 65 and older. Although it has been proven that there is an increase in titers, the differences in the efficacy of the vaccines have yet to be determined. All hospital, clinic, and LTCF personnel and residents should receive the annual seasonal influenza vaccine. There is strong evidence that the vaccination of staff, even in the event of patients/residents not being vaccinated, can decrease mortality of elderly patients.

A study in the United Kingdom looked at LTCFs that adopted a policy for influenza vaccination of staff without changing resident vaccination policies compared to control facilities without this policy. Vaccination of staff was promoted by lead nurses, leaflets, posters, and vaccination sessions. Over the 2-year study in intervention LTCFs the percentage of vaccinated staff was 48.2% and 43.2%, and in control facilities was 5.9% and 3.5%. There was a statistically significant difference among the number of deaths, influenza-like illness, general practitioner consultations, and admissions of residents to the hospital with influenza-like illness. Both the World Health Organization and Centers for Disease Control and Prevention (CDC) recommend annual vaccination for individuals age 65 and older. This recommendation is for the elderly in both the LTCF and community setting. A meta-analysis showed that vaccination of community-dwelling adults older than 65 led to a decrease in influenza-like illness, hospitalization for pneumonia and influenza, and mortality following hospitalization for pneumonia and influenza.

An influenza outbreak in a LTCF is generally defined as two or more residents developing respiratory illness within 72 hours of one another or one laboratory confirmed positive case in a resident with other residents showing signs of respiratory infection. Although rare, influenza outbreaks can occur outside of influenza season. Influenza testing should be included when testing for other respiratory pathogens during an outbreak outside of flu season.

Other than vaccination, other methods to prevent the spread of influenza include posting signs about cough etiquette, hand-washing technique, provision of tissues and receptacles, face masks for those with respiratory symptoms, and easily accessible alcohol-based hand sanitizer. Healthcare personnel with symptoms of respiratory illness should be instructed to stay home from work or be removed from direct patient care activities. Visitation for hospitalized patients with influenza should be minimized to limit the spread of infection.

In the event of an outbreak, daily surveillance of new cases or possible exposures should be initiated. Standard precautions and droplet precautions should be initiated. Antiviral treatment for those with suspected influenza should begin immediately, without waiting for a laboratory confirmation. All healthy residents in LTCF, as well as staff, should receive chemoprophylaxis in a facility where an outbreak is occurring. In the hospital setting, a plan should be in place to hasten the administration of the influenza vaccine to appropriate patients. Influenza
outbreaks should be reported to local or regional health departments.

A definitive diagnosis of influenza is based on the results of a polymerase chain reaction (PCR) analysis; however, many health centers, whether LTCFs or primary care centers, do not have access to real-time PCR analysis. As such, rapid influenza diagnostic tests (RIDTs) have become increasingly popular. They offer a simple test that can be performed at bedside with quick results. A study of 107 patients analyzed two separate RIDTs from patients with suspected H1N1 influenza and compared them to real-time PCR results of the same specimens. They found that the RIDTs had a high specificity, moderate sensitivity, and a negative predictive value of 80%. Thus, positive RIDT results with a suspected presentation of influenza do not require confirmation of diagnosis by PCR, but false negatives are common. Those who have negative test results with a high clinical suspicion of influenza should be treated as a positively-tested patient until negative results are confirmed by PCR analysis. Another limitation to the rapid antigen tests is that the viral load may not be detectable by the test early in the course of the infection. The sensitivity of rapid antigen testing was found to be significantly lower, within 3 hours of onset (56%), compared to more than 4 hours from onset (>80%). RIDTs are available for both A and B strains of influenza, but the limit of detection varies among different strains and different test manufacturers.

Treatment depends on the severity of illness as well as where the elderly individual resides. Outpatient treatment recommendations indicate that all those age 65 and older with suspected influenza receive empiric therapy, regardless of symptom severity or immunization status. Ideally, treatment should be started within 48 hours of symptom onset, as viral load begins to decrease within 24 to 48 hours after symptom onset. However, in immunocompromised patients or patients at risk for severe complications (such as the elderly or those with comorbidities), the viral load may act differently. In hospitalized patients, antiviral treatment should be started on admission regardless of time since start of symptoms. Studies that look at initiation of therapy past 48 hours still show some benefit in terms of mortality, severe complications, and improved clinical outcomes. The CDC recommends that when an influenza outbreak occurs in a LTCF all eligible residents should receive prophylactic antiviral therapy, regardless of immunization status.

The recommended drugs for those over 65 are generally the same as for younger persons. Nursing facility–specific evidence suggests that treatment with oseltamivir has been associated with decreased risk of death among residents during an influenza outbreak and reduced length of hospital stay. In the case of renal dysfunction, the dose should be adjusted to 75 mg once daily if creatinine clearance is 10–30 mL/min because of increased serum concentrations of oseltamivir’s active metabolite. The duration of oseltamivir for treatment is 5 days, but longer courses can be considered if after 5 days the patient remains severely ill. For prophylaxis, the 75 mg once daily dose is reduced to 75 mg by mouth every other day if creatinine clearance is 10–30 mL/min. The length of prophylactic therapy depends on the type of exposure. Although a duration of 10 days is usually recommended for household exposure and 7 days if other exposure, due to close quarters and the immunocompromised nature of LTCF residents, a minimum duration of 2 weeks is recommended for a patient in a hospital or LTCF or up to 10 days after the most recent case identified, whichever is longer. Oseltamivir has not been studied in individuals with liver disease.

Zanamivir does not require renal dose adjustment and has not been studied in liver disease. However, a study of its safety in animals did not find significant systemic toxicity at exposures greater than 100-fold higher than those that would be experienced with normal clinical use. Zanamivir may be difficult to inhale for patients with COPD, asthma, or other respiratory complications.
KEY POINT: There is a difference in duration of influenza therapy for elderly patients dwelling in the community versus those who reside in LTCFs.

**Barriers in Treatment of the Geriatric Population**

The absence of fever or respiratory symptoms may lead healthcare providers to dismiss influenza as a diagnosis until more severe symptoms develop, delaying treatment and increasing the risk of complications, such as pneumonia. Even in a patient with respiratory symptoms, treatment may be delayed by a misdiagnosis of respiratory tract infection or a cold. Body aches from influenza infection may be confused with arthritis, and altered mental status may be confused with worsening of cognitive function. Comorbidities, such as COPD and congestive heart failure, may also present with pulmonary symptoms during exacerbation, so they may confound appropriate diagnosis of influenza. Increased incidence of dementia and depression in the elderly may make it difficult for an elderly patient to describe symptoms or desire treatment. Timing of antiviral administration is crucial. If a LTCF does not have preapproved orders to initiate antiviral drugs, treatment may be delayed until a physician can see patients at the facility. This type of delay could lead to spread of the virus to more residents and complicate the outbreak further. Pre-approved medication orders and standing orders for influenza vaccine administration during flu season should be in place. An institutional influenza protocol, perhaps authored by the institution’s pharmacy or consultant pharmacist, may be beneficial to initiate treatment as soon as possible.

Influenza diagnosis may be delayed by confusion of influenza with the common cold. Onset of influenza is abrupt: a patient may feel fine in the morning but feel very ill by evening. A cold comes on more gradually. Influenza is also typically associated with high fevers and severe muscle aches. Additionally, pneumonia and influenza, given their somewhat similar presentations, are often confused at diagnosis. Similar symptoms include fever, chills, cough, headache, and loss of appetite. Pneumonia tends to have a more gradual onset and manifests with labored breathing and productive cough. Physical examination may reveal rhonchi or rales. Although a vaccine is available, influenza remains an extremely contagious illness with a high rate of life-threatening complications.

KEY POINT: An absence of respiratory symptoms should not lead to the exclusion of influenza as a diagnosis.
**Case 1: Antibiotic Stewardship**

**Subjective:**
A CNA in an LTCF reports to the charge nurse that JP, a 79-year-old male resident of the Alzheimer unit, has had a change from baseline status. She reports that he is more lethargic and confused, and she is concerned that this morning JP voided a small amount of dark, foul-smelling urine. The charge nurse replies “Well, we’ve seen this before, haven’t we?” and goes to assess JP. He is rather uncooperative this morning and gruffly tells her “leave me alone, I don’t feel good.” He does not provide another reliable self-report, but the charge nurse confirms the findings of the CNA and assesses JP’s temperature to be 98.8°F. She places a call to the mid-level practitioner, who follows JP and requests an order to obtain a urinalysis, reporting change in mental/functional status, change in urine quality, and complaint of constitutional symptoms. She adds that JP has had a history of recurrent UTI, with two other episodes since his admission to the facility 4 months ago.

**Objective:**
PMH: Alzheimer disease, hypertension, recurrent UTI. Vitals: BP 108/60 mmHg, P 98 BPM, RR 18, T 98.8°F.

**Medications:**
Donepezil 10 mg by mouth every day at bedtime, hydrochlorothiazide 25 mg by mouth daily, multivitamin by mouth daily.

**Assessment:**
This patient is displaying an atypical presentation of possible UTI. Although infection is suspected, the potential for other illnesses should be evaluated and excluded. The data provided in the charge nurse’s report are certainly supportive of a possible UTI, but the report does not contain enough data to differentiate other causes of illness.

**Plan:**
1. The nurse practitioner orders a CBC, a complete metabolic panel, and a urinalysis with culture and sensitivity.
2. She also requests additional patient assessment data over the phone, including vitals data (other than just body temperature), an assessment of skin/mucous membranes, and subjective data regarding appetite and oral intake.
3. She requests that the charge nurse fax some chart data providing records of the previous UTI occurrences, including culture and sensitivity reports, and previous medication orders for antibiotic therapy and the associated dose, regimen, and duration.

**Rationale:**
JP may have a UTI, but the data provided in this exchange of information are not comprehensive enough to determine that UTI is probable. The charge nurse has made a reasonable assumption regarding the suspected diagnosis, based on the patient’s recent history. However, providing data supportive of this assumption rather than a full patient assessment report could lead to misdiagnosis and inappropriate treatment in the event another problem is the root cause. The nurse practitioner is wise to request additional data instead of granting the order for a urinalysis alone.

The patient’s presentation would not necessarily satisfy updated stricter recommendations for applying the McGreer criteria. Therefore, when there is less confidence in the assessment based on the clinical presentation, the pursuant diagnostic testing is warranted. This is especially important because there is a high probability that the urinalysis
would yield bacteriuria, regardless of whether the patient was symptomatic or not. By ordering a CBC, complete metabolic panel, and other patient assessment data in addition to the urinalysis, other possibilities can be evaluated. These tests can not only help confirm/refute a UTI but will reveal data regarding other etiologies; for instance, dehydration. It is possible that the “recurrent UTI” history, which predisposes the charge nurse to assume UTI now, is actually another ongoing problem that would not be expected to resolve with repeat courses of antibiotics. Alternatively, if a UTI is what JP is experiencing, the additional data will be crucial to selecting appropriate therapy. Not only will data from the chemistry panel assist with an estimate of renal function, but records providing history about the prior UTIs, the organisms involved, their sensitivity patterns, the antibiotics selected, and their doses and durations of therapy can shed light on whether JP is truly experiencing recurrence or whether this relapse is due to inappropriate antibiotic selection, subtherapeutic dose or duration, or perhaps even suggest an unrecognized prostatitis.

Case Summary:
This case illustrates an opportunity for antibiotic stewardship. It describes a fairly common scenario of communication between on-site hands-on caregivers and a remote provider and demonstrates just how easily shortcuts in data reporting might make it difficult to accurately assess suspected infection. The charge nurse is concerned about her patient and wants an intervention as soon as possible, and it is expedient to simply allow the requested urinalysis order. However, the stewardship behaviors demonstrated by the nurse practitioner in this case were best practice. Although it is true that the additional tests and records review add a phlebotomy component, additional cost, and additional assessment time, there is a strong argument to be made that the costs associated with these steps are offset by the potential value of a more accurate diagnosis; a more targeted, effective intervention; and avoidance of iatrogenic harm associated with inappropriate or unnecessary treatment.
Case 2: Atypical Disease Presentation

Subjective:
In mid-September, the activities coordinator of a LTCF asks the charge nurse why HB, an 84-year-old female resident of the facility, hasn’t been attending any events lately. She reports that HB usually attends every event available and is very active in the community, but she hasn’t seen her the past 2 days. The charge nurse finds out that HB is complaining of shortness of breath and didn’t eat well yesterday. The medication administration record shows no missed doses of diuretics or any other medication changes. HB states that she just doesn’t feel good and is too congested and too tired to go out and socialize. The charge nurse hears rales in HB’s lung bases on auscultation, but there is no chest x-ray available at the facility. One of the CNAs reports that BE, an 80-year-old female that is good friends with HB, has also been feeling under the weather. The charge nurse calls one of the facility’s physicians and reports the change in status. The physician orders a CBC, a complete metabolic panel, a brain natriuretic peptide (BNP) level, and a RIDT. He also requests a physical exam of HB, including checking for peripheral edema and jugular venous distention. He also asks for HB’s weight, with a comparison to her last weight taken.

Objective:
Wt: 79.4 kg compared to 80.3 kg 2 months ago. PMH: hypertension, breast cancer, diabetes mellitus type 2, systolic heart failure, osteoarthritis. Vitals: BP: 123/74 mmHg, P 75 BPM, RR 21, T 99.6°F.

Medications:
Lisinopril 40 mg once daily, metformin 1,000 mg twice daily, furosemide 40 mg once daily, metoprolol ER 25 mg once daily, acetaminophen 325 as needed for arthritic pain. Immunization history not clearly documented in the clinical record. Rapid influenza diagnostic test: positive.

Labs:
WBC: 14,200/mm³, SCr 1.2 mg/dL, CrCl 31.4 mL/min, BUN 16 mg/dL, BNP 256 pg/mL.

Assessment:
1. The physician feels that due to HB’s respiratory symptoms and the fact that another resident in close proximity to HB is feeling poorly that an infectious cause should be considered. He consults the pharmacist to decide whether both HB and BE should be treated for influenza or whether he should take them to the hospital to do a PCR test to ensure the diagnosis.
2. HB is showing influenza symptoms that can easily be confused with an exacerbation of her pre-existing heart failure. The cause of her shortness of breath, fatigue, and change in appetite could be due to fluid overload, but it was wise of the physician to consider the possibility of an infectious cause given the time of year and the fact that another resident in close proximity to HB is feeling poorly.

Plan:
1. The pharmacist requests that other residents be monitored for development of respiratory symptoms and that BE have a RIDT performed. She educates the staff that a rapid influenza test may result in a false negative, so a negative result is not a valid reason to withhold influenza treatment if other chronic disease exacerbations are ruled out.
2. The pharmacist orders treatment of influenza for HB of oseltamivir 75 mg by mouth twice daily for 5 days. After 5 days, the need to continue therapy will be re-evaluated based on her response to therapy.
3. The pharmacist asks the physician for standing orders for oseltamivir for residents that begin to display respiratory illness and also asks that the residents of HB’s wing as well as staff begin prophylactic treatment with oseltamivir 75 mg once daily for patients with CrCl greater than 30 mL/min and 75 mg by mouth every other day for those with CrCl of 10–30 mL/min. She states that the prophylaxis should be continued for a minimum of 2 weeks or 10 days after the last case of influenza is identified, whichever is longer.

4. Visitation to HB’s wing is minimized to lower the risk of spreading infection. Daily surveillance and droplet precautions are put in place. A program for influenza vaccination for the current year is to begin immediately given that it is mid-September and the new vaccine is now available.

5. The pharmacist and Director of Nursing discuss the implementation of an immunization history section to be added to the medical record that will not be thinned for records archiving. All facility residents without a clear vaccination history will be offered immunization.

Rationale:
HB may have the flu or may be experiencing an exacerbation of another disease. The information given at this point does not lead to a definitive diagnosis of influenza, but HB’s age would make her high risk for complications due to influenza, so the physician request for a RIDT and monitoring of other residents is a sensible choice. This is especially important because her vaccination history is unclear. It may be a good recommendation to ask around for other residents feeling poorly and test for influenza in those individuals as well. Given that HB is social in the community, she may have spread the virus to others. The rapid diagnostic test may not be definitive, but if HB is not retaining fluid and heart failure exacerbation can be ruled out, it may be beneficial to begin antiviral treatment.

Case Summary:
This case illustrates the difficulty of diagnosing influenza in a setting where other disease states can present similarly. Although it is practical to rule out other causes of symptoms, influenza treatment should not be delayed. In an LTCF, where multiple providers may have different styles of charting, there can be inconsistencies in how some patient history data (such as immunization status) are maintained. Given the risk of infectious disease spread, a specific, dedicated place for immunization history to be maintained and reliably located is important.
Many factors affect risk for and vulnerability to infection among older persons. These include age-related changes in the immune system, functional status, comorbidities, and living environment. The desire to eradicate an infection that could be a significant source of either morbidity or mortality often leads to aggressive therapy with antibiotics. Yet, inappropriate use of antibiotics is also a risk factor for adverse outcomes, including the proliferation of *C. difficile*–associated diarrhea and antibiotic resistance. Therefore, a balance must be struck between adequately identifying and reacting to signs of severe infection and minimizing antibiotic use in situations in which they may not be indicated. On balance, this means early recognition and aggressive treatment of more deadly infections, such as pneumonia, while scrutinizing the accuracy of more commonly occurring diagnoses, such as UTIs. Among older persons, antibiotic stewardship not only implies infection control and appropriate use of antibiotics. It also involves a careful, deductive approach to the differential diagnosis, an understanding of the limitations of general surveillance criteria in some settings, and the application of modified criteria for assessing fever and other symptoms.

Once an infection diagnosis has been established, the general approach to treatment does not differ for older versus younger populations. However, the clinician must be mindful of the need to select dosages that are appropriate for the patient’s pharmacokinetic parameters, and to use clinical judgment when interpreting bedside estimates of creatinine clearance. In severe infections, it may be better to lean toward the higher antibiotic dose, or to at least preserve the initial or loading dose, to ensure rapid attainment of therapeutic concentrations. The multi-venue nature of care for the older population means that optimal infection control and antibiotic stewardship is a common responsibility of all health professionals in all healthcare settings, not only to ensure optimal outcomes for today’s population of older patients, but for the generations that follow.

**Clinical Pearls**

- Although CXRs are recommended to confirm a diagnosis of pneumonia, the patient’s venue of care or advance directives may preclude transfer to a hospital or access to this test. Due to the necessity of initiating antibiotics as quickly as possible, diagnosis may have to be based on clinical presentation. Scoring tools that evaluate factors such as presence of fever, elevated WBC count, respiratory rate, or cognitive status can increase the likelihood of accurately identifying pneumonia.

- Atypical disease presentation can make it difficult for the clinician to differentiate signs of respiratory conditions such as COPD from other conditions, such as heart failure. Older patients may be vulnerable to receiving medications directed at symptoms without a clear diagnosis of the underlying cause. When drug regimen review reveals the use of breathing treatments such albuterol or ipratropium nebulizers for shortness of breath in combination with medications such as furosemide for edema, a diagnostic evaluation to confirm the root cause and initiate the appropriate evidence-based therapy is necessary.
Self-Assessment Questions

1. What are the most important age-related changes in the immune system, and what are the consequences of these changes?

2. Which types of infections are most common among frail populations, and which types carry the greatest mortality risk?

3. What is the optimal criteria for determining fever in an elderly patient?

4. How might modification of UTI diagnosis criteria help avoid use of antibiotics for asymptomatic bacteriuria?

5. What types of antibiotic stewardship interventions are most likely to result in reduced utilization of antibiotics?

6. What is the most appropriate approach to the adjustment of antibiotic dose for a patient with renal impairment?

7. What factors can be used to support a diagnosis of pneumonia when a CXR cannot be obtained?

8. When is nasopharyngeal testing for influenza indicated in the long-term care setting?

9. How does the dose or duration of antiviral therapy for influenza differ for elderly patients?

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